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(ZHURNAL OBSHCHEI KHIMII)

IN ENGLISH TRANSLATION

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ENTHALPY OF FORMATION OF COMPOUNDS OF TITANIUM WITH ELEMENTS OF THE MAIN SUBGROUP OF GROUP V

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Of all the compounds of titanium with elements of Group V subgroup, only the nitride has been characterized thermochemically [1].

As starting materials for the present investigation we used metallic titanium in the form of a sponge (prepared in the laboratory and containing 99% Ti), red phosphorus, carefully washed free from traces of oxides and acids with water and then dried to constant weight, distilled arsenic and metallic antimony and bismuth, which, according to spectral analysis, contained very small amounts of other elements (representing a total of tenths of a percent).

For the preparation of titanium phosphide, a certain amount of titanium was placed in a boat in a quartz tube, to which was also added an excess of red phosphorus; the tube was carefully evacuated to 10^{-4} mm Hg, sealed and heated in a tubular furnace in such a way that the boat with the titanium was at 900°, while one of the ends of the tube was outside the furnace and heated with a gas burner to a temperature which ensured that there was a sufficiently high phosphorus vapor pressure in the tube. The synthesis lasted for 60-65 hours. Titanium arsenide was also prepared in the same way.

The preparations obtained contained a certain excess of phosphorus or arsenic, which was removed by heating in vacuum at 600-650°. The titanium content of the titanium phosphide or arsenide preparations was determined volumetrically [2].

Found %: Ti 60.34. TiP. Calculated %: Ti 60.28. Found %: Ti 39.87, 38.85, 39.83. TiAs. Calculated % Ti 39.00.

Titanium antimonide, TiSb, was prepared in the following way: titanium and antimony, taken in stoichiometric ratios, were carefully mixed and compressed into tablets. The latter were placed in a quartz ampoule, which was evacuated to 10^{-4} mm Hg, sealed and placed in a muffle. The ampoule was first heated uniformly to 900° for 8-10 hours and then at 1000° for 18-20 hours. After this, the ampoule was slowly cooled. Determination of the titanium and antimony content of the preparation obtained showed that no change occurred in the ratio of the components during fusion.

X-ray pictures of the preparations showed interplanar distances close to those reported in the literature (Table 1).

An attempt to prepare titanium bismuthide was not successful, as even at 500° the titanium bismuthide decomposed to the free components and at lower temperatures the reaction proceeded very slowly.

The heats of formation were found as the difference in the heats of combustion of stoichiometric mixtures and the compounds under identical conditions.

The heats of combustion were determined in a precision vacuum calorimeter described previously [6]. The data obtained are presented in Table 2.

TABLE 1

Lattice Parameters of Titanium Phosphide, Arsenide and Antimonide (in A)

Parameter	TiP		TiAs		TiSb	
	our data	literature[3]	our data	literature[4]	our data	literature[5]
a	3.48	3.487	3.63	3.635	3.98	3.97
c	11.62	11.65	12.03	12.04	6.17	6.18
c/a	3.33	3.34	3.31	3.31	1.55	1.55

TABLE 2

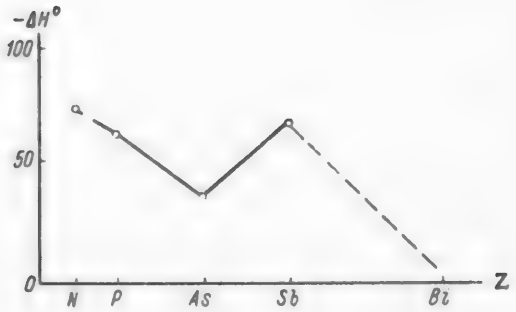
Heats of Combustion of Compounds and Corresponding Mixtures and Heats of Formation

Substance combusted	Heat of combustion of comp. or corresponding amt. of stoich. mixt. of components (in kcal/g-formula)	Heat of formation of compound (in kcal/g-formula)
TiP	330.9	63.5
	330.3	64.1
	331.7	62.7
Average	331.0	63.4
Mixt. (Ti + P)	394.6	
	394.3	
	394.3	
Average	394.4	
TiAs	259.9	36.4
	260.5	35.8
	261.2	35.1
Average	260.5	35.8
Mixt. (Ti + As)	295.9	
	295.5	
	297.5	
Average	296.3	
TiSb	249.8	66.7
	248.7	66.8
	249.4	67.1
Average	249.3	67.2
Mixt. (Ti + Sb)	316.6	
	317.0	
	316.0	
Average	316.5	

$Ti_{cryst} + P_{cryst} = TiP_{cryst}$: $\Delta H^0 = -63.4 \pm 0.5$ kcal/g-formula

$Ti_{cryst} + As_{cryst} = TiAs_{cryst}$: $\Delta H^0 = -35.8 \pm 0.05$ kcal/g-formula

$Ti_{cryst} + Sb_{cryst} = TiSb_{cryst}$: $\Delta H^0 = -67.2 \pm 0.5$ kcal/g-formula



Dependence of heats of formation of titanium compounds with elements of the main Group V subgroup on the atomic numbers of the latter.

According to x-ray investigation, the combustion products of the compounds and the corresponding mixtures were identical. As is known, titanium does not burn completely to TiO_2 under the conditions of calorimetric experiments (the usual combustion product has a composition corresponding to the formula $TiO_{1.95}$-$TiO_{1.98}$) [7]. We cannot exclude the possibility that in the combustion of the mixtures and the compounds, the degree of oxidation of the titanium may have been somewhat different. This could have led to a slight error in the final result. In any case, this error cannot have altered the formula for the dependence of the heats of formation of titanium compounds with elements of the main Group V subgroup on the atomic numbers of the latter. The character of this dependence is illustrated by the figure.

It is readily seen that the course of the heats of formation obeys the rule of secondary periodicity [8, 9]: the slight fall in the heat of formation in going from TiN to TiP is followed by a considerably sharper fall to TiAs and then an increase to TiSb. Considering the fact that we found the compound of titanium with bismuth to be unstable, it can be assumed that the transition from TiSb to TiBi is accompanied by a sharp fall in the heat of formation.

In connection with the results of previous work [9], it was established that among the compounds of elements of the main Group V subgroup with metals, the course of the heats of formation of compounds with metals of the subsidiary subgroup (Zn, Cd and Ti) clearly obeyed the rule of secondary periodicity. The course of the heats of formation of compounds of elements of the main Group V subgroup with active metals of the main subgroups Mg, Ca, Sr, and Li [9] is not typical of secondary periodicity, although it is not always monotonic.

SUMMARY

1. The values of the enthalpies of formation of compounds of titanium with elements of the main Group V subgroup were established.

2. It was established that the course of the enthalpies of formation in the series TiN–TiBi obeys the rule of secondary periodicity.

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ENTHALPY OF SOLUTION OF ZINC PERCHLORATE HEXAHYDRATE

S. A. Shchukarev, S. N. Andreev, and Z. U. Borisova

A knowledge of accurate values of the enthalpies of solution of various crystal hydrates is essential for developing the thermodynamic theory of the solubility of salts and also for understanding the chemical nature of the crystal hydrates themselves. As far as we know, no information has appeared in the literature up to now on the enthalpies of solution of $Zn(ClO_4)_2 \cdot 6H_2O$; the present article is devoted to this subject.

The enthalpy of solution was determined in a microcalorimeter operating on the dilatometric principle [1]. The calorimeter was calibrated using potassium chloride [2, 3]. The average value of one division of the calorimeter capillary equaled 0.0254 ±0.002 cal.

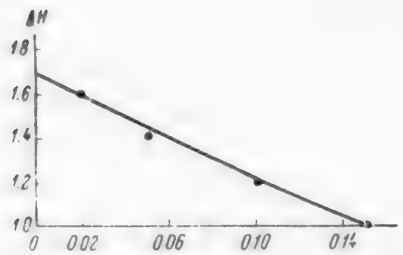

Fig. 1. Dependence of enthalpy of solution of $Zn(ClO_4)_2 \cdot 6H_2O$ on the amount of mother solution added.

TABLE 1

ΔH of Solution of $Zn(ClO_4)_2 \cdot 6H_2O$ at a Dilution of 1:200

Drying time (in days)	ΔH (in kcal/mole)	Error (in %)
0	1.6±0.1	7
1	1.73±0.03	2
3	1.69±0.05	3
10	1.62±0.06	4
30	1.59±0.05	3

Zinc perchlorate hexahydrate was prepared by dissolving zinc carbonate in perchloric acid. The salt obtained was recrystallized 4-5 times. After each recrystallization, the value of the enthalpy of solution was checked; it ceased to change after 3 recrystallizations. The salt was analyzed for zinc content by titration with Trilon B in an ammonium buffer solution in the presence of the indicator Acid Chrome Dark Blue. The accuracy of the analysis was ±0.02%.

Since, on sucking off the filtrate on a Buchner funnel, the crystal hydrate was always obtained together with a small amount of mother solution, it was necessary to carry out thermochemical experiments allowing for possible additional effects, depending on the presence of this mother solution. In connection with this, we were obliged to carry out an additional investigation: using a dilution of 1:200, we measured the enthalpies of solution of the solid hexahydrate, to which was purposely added a certain amount of mother solution. Figure 1 shows the values obtained, calculated for 1 mole of $Zn(ClO_4)_2 \cdot 6H_2O$ and allowing for the part of this mole, which was present in the mother solution impregnating the sample of crystals. The values of the enthalpy of solution lay (within the limits of experimental error) on a straight line; extrapolation of the line to a zero content of mother solution gave the value of the enthalpy of solution of the completely dry crystal hydrate, which equaled +1.70 kcal/mole.

As a check, we determined the enthalpy of solution of zinc perchlorate hexahydrate, freed from mother solution by careful centrifuging. In this case, samples corresponding in analysis to a content of 6.00 molecules of water gave, on an average, an enthalpy of solution value of 1.73 kcal/mole; the deviation in the values of the enthalpy of solution of a preparation obtained by this method reached 7%.

TABLE 2

ΔH of Solution of $Zn(ClO_4)_2 \cdot 6H_2O$ at Various Dilutions (the values were the average of 8-10 experiments)

Dilution	Δ H (in kcal/mole)	
1 : 1000	+1.40	
1 : 700	+1.40	
1 : 500	+1.40	
1 : 200	+1.73	
1 : 100	+1.80	
1 : 75	+1.85	
1 : 50	+1.90	
1 : 30	+1.95	±0.03
1 : 20	+2.22	
1 : 16	+2.46	
1 : 13	+2.71	
1 : 11	+2.97	
1 : 9	+3.32	
1 : 8	+3.55	
1 : 7	+3.75	

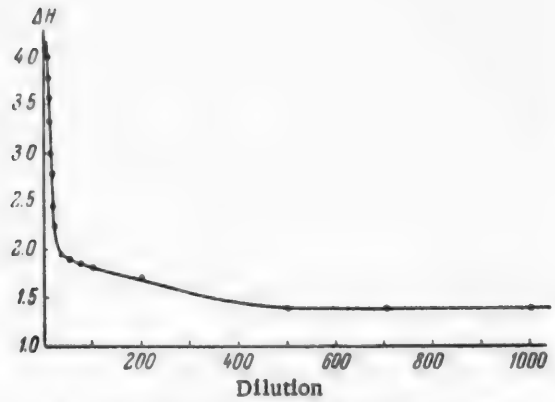

Fig. 2. Enthalpies of solution of $Zn(ClO_4)_2 \cdot 6H_2O$ at various dilutions.

The mother solution could also be removed by drying over sulfuric acid; however, we could not exclude the possibility that a lower hydrate would be partially formed in this case. We measured the enthalpies of solution of hexahydrate, kept over sulfuric acid for various times; the calorimetric measurement was accompanied by analysis of the preparation investigated.

Data obtained in these experiments are given in Table 1.

As the data in Table 1 show, the solution of freshly precipitated zinc perchlorate hexahydrate, containing a slight excess of mother solution, gave comparatively low values for the enthalpy of solution. As would be expected, the excess mother solution numerically lowered the endothermal effect of solution of the salt since the enthalpy of dilution of the saturated solution was exothermal.

The perchlorate hexahydrate, dried for a day and containing 6.00 molecules of water, gave the maximum enthalpy of solution, close in value to that measured by the method described above. With further drying of the hexahydrate, the enthalpy of solution decreased numerically and this may be explained by partial dehydration of the crystals with the formation of a lower hydrate, dissolving noticeably more exothermally. The data presented actually show that even very slight dehydration, lying almost within the limits of analysis error, led to a considerable fall in the enthalpy of solution.

On the basis of the experimental data presented, we arrived at the conclusion that a preparation dried for a day over sulfuric acid was most suitable for determining the enthalpy of solution. All subsequent work was carried out with this preparation and the samples were taken in a dry chamber over concentrated sulfuric acid.

The values obtained for the enthalpy of solution at various dilutions are presented in Table 2 and Fig. 2.

According to the data in [4], the dilution of 1 mole of hexahydrate to 7 moles of water corresponds to a saturated solution. The first integral enthalpy of solution was found to be equal to 1.40 kcal/mole. The endo-effect of solution increased in value as the dilution decreased; in going from infinitely dilute solutions to a saturated one, the enthalpy of solution changed by 2.35 kcal/mole.

SUMMARY

1. The enthalpies of solution of zinc perchlorate hexahydrate in water at dilutions of from 1 : 1000 to 1 : 7 were determined.

2. The value of the first integral heat of solution was found to equal +1.40 kcal/mole.

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ENTHALPY OF FORMATION OF VANADIUM OXIDES

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The samples of vanadium oxides required for the investigation were prepared by sintering mixtures of hydrogenated vanadium powder with vanadium trioxide, compressed into tablets, in a high frequency furnace at 1600° in high vacuum (for 2 hours). The preparations obtained were analyzed by determining the increase in weight when they were oxidized to V_2O_5.

X-ray investigations of the preparations showed that the region of homogeneity of vanadium monoxide obtained under these conditions was over the range $VO_{0.86}$-$VO_{1.27}$.

The heats of combustion of the vanadium oxides were determined on small samples (0.1-0.2 g) at an oxygen pressure of 42 atm in a vacuum calorimetric apparatus described previously [1] with the difference that the calorimetric bomb weighed only 7 kg (so that the rise in temperature was sufficient with the combustion of small samples). Under the collodion bag with the sample of the preparation was placed a corundum crucible, closed with small corundum plates with openings. The fused mass of oxides fell onto these plates and then dripped into the crucible through the openings in them; this improved its contact with oxygen.

The empirical composition of the combustion product was determined by the increase in weight on oxidation. For vanadous oxide with an oxygen content less than that of $VO_{1.23}$ it reached $VO_{2.30}$-$VO_{2.35}$; oxides with a higher oxygen content were combusted only to $VO_{2.20}$. The correction for the incompleteness of combustion was introduced on the assumption that the combustion product was a mixture of $VO_{2.0}$ and $VO_{2.5}$. A preparation with the composition $VO_{1.509}$ burned badly and therefore it was burned in a mixture with $VO_{1.003}$, whose heat of oxidation we determined previously. The results of determining the heats of combustion (Q_p) of vanadium oxides and metallic vanadium (with appropriate corrections) and the enthalpies of formation of vanadium oxides ($-\Delta H^\circ_{form}$) of various compositions calculated from them are presented in Table 1. In this table, the errors are evaluated without allowing for the error in determining the enthalpy of formation of $VO_{2.5}$. For determining the form of the dependence of the enthalpy of formation of vanadous oxide on composition, this was justifiable since the total error was not important in this case, but the error with which we determined the enthalpy of formation of the separate oxides.

In calculating the total error, it was necessary to consider the error of all the values used for the calculation. Since the enthalpy of formation of $VO_{2.5}$ was given with an error of ±1 kcal, then the total error in the enthalpies of formation of all the other vanadium oxides, VO_{1+x}, could not be less than ±1 kcal.

Up to now, the enthalpy of formation of vanadium oxides has been determined for VO, V_2O_3, VO_2 and V_2O_5. However, due to the difficulties associated with determining the heats of combustion of vanadium oxides, the data of different authors differ quite considerably. In Table 2, our data are compared with those available in the literature.

Considering the errors given by different authors, it can be stated that our values agree well with those of Siemonsen and those recommended by the U. S. Bureau of Standards (the latter considers the most reliable the values presented by Siemonsen, with some refinement of them, and therefore their error should evidently be taken as that given by this author).

TABLE 1

Enthalpies of Formation of Vanadium Oxides

Composition of preparation	Heat of combust. (in kcal/g-form.)	Correction for incompleteness of combustion (in kcal)	Corrected heat of combustion (in kcal/g-formula)	Q_p (in kcal/g-form.)	$-\Delta H_{form}$ (in kcal/g-form.)	Average value of $-\Delta H^\circ_{form}$	$-\Delta H^\circ_{form}$ of mixt. of $VO_{1.00}$ and $VO_{1.50}$ (kcal/g-form)	Difference (in kcal)
V	183.1, 185.6	2.9, 2.3	186.0, 187.9	186.7, 188.6				
$VO_{2.50}$	—	—	—	—	186.7, 188.6	188±1		
$VO_{1.509}$	33.5, 28.5	6.5, 7.3	40.0, 35.8	40.3, 36.1	147.7, 151.9	150±2		
$VO_{1.522}$	41.6, 46.9	10.9, 8.4	52.5, 55.3	52.8, 55.6	135.2, 132.4	134±2		
$VO_{1.280}$	45.5, 47.0	9.7, 9.4	55.2, 56.4	55.6, 56.8	132.4, 131.2	131.8±0.6		
$VO_{1.230}$	52.5, 51.4	11.4, 11.3	63.9, 62.7	64.3, 63.1	123.7, 124.9	124.3±0.6	123.6	+0.7
$VO_{1.188}$	59.3	8.7	68.0	68.4	119.6	119.6±0.6	119.7	—0.1
$VO_{1.176}$	59.6	9.3	68.9	69.3	118.7	118.7±0.6	118.5	+0.2
$VO_{1.004}$	71.4, 70.2, 69.2	5.9, 5.4, 7.9	77.3, 75.6, 77.1	77.7, 76.0, 75.5	110.3, 112.0, 110.5	110.9±0.7	110.8	+0.1
$VO_{1.047}$	74.2, 75.1	4.9, 4.9	79.1, 80.0	79.5, 80.4	108.5, 107.6	108.0±0.5	106.7	+1.6
$VO_{1.003}$	83.2, 79.0, 77.2	3.7, 5.1, 8.1	86.9, 84.1, 85.3	87.3, 84.5, 85.7	100.7, 103.5, 102.3	102±1		
$VO_{0.945}$	84.7, 84.9	4.5, 6.4	89.2, 91.3	89.7, 91.8	98.3, 96.2	97.1		
$VO_{0.904}$	89.3, 88.8	4.3, 4.6	93.6, 93.4	94.1, 93.9	93.9, 94.1	94.0±0.6		
$VO_{0.855}$	91.2, 91.0	5.7, 6.1	96.9, 97.1	96.4, 97.6	90.6, 90.4	90.5±0.6		

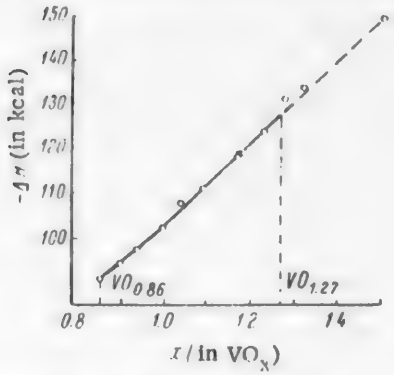
TABLE 2

Enthalpies of Formation of Vanadium Oxides ($-\Delta H^\circ_{form}$ in kcal) According to the Data of Various Authors

Composition	Siemonsen [2]	Kubashevskii [5]	U. S. Bureau of Standards [4]	A. F. Kapustinskii [3]	Our data
VO		106±6	100	115	102±1
V_2O_3	296±2	300±9	290	320	300±4
V_2O_4	342±2	352±14	344	375	
V_2O_5	373±2	382±12	373	437	376±2

The figure shows the composition dependence of the enthalpy of formation of vanadium oxides. The data in Table 1 shows that the enthalpy of formation of substances with the composition $VO_{1.00}$-$VO_{1.27}$ ($VO_{1.27}$ is the

upper limit of the region of homogeneity of vanadous oxide) hardly differs from the enthalpy of formation of mixtures of $VO_{1.00}$ and $VO_{1.50}$ of the same empirical composition. With one exception, the difference between these values corresponds to our experimental error. The exception is probably the result of a random experimental error. A similar rule was previously established for titanous oxide, TiO_{1+x} [1] and ferrous oxide, FeO_{1+x} [6]. In all these cases the enthalpy of formation of MeO_{1+x} from $MeO_{1.00}$ and $MeO_{1.50}$ was imperceptibly small. This rule agrees with previously proposed ideas [1,7] on the chemical structure of lattices of certain compounds of variable composition. Actually, even when two oxides form some intermediate oxide which has a certain definite structure, within whose limits atoms of an element of a subsidiary subgroup in different valence states are distributed uniformly in the lattice, then the enthalpy of this process is comparatively small in absolute value (1-4 kcal). With the formation of a submicro-heterogeneous structure,* the thermal effect must be considerably less, since basically the heat effect of the formation of an oxide of intermediate composition from two oxides is determined by the change in energy of the electrostatic interaction and the change in energy of the exchange interaction between atoms of the element of the subsidiary subgroup. The latter value cannot be appreciable in the formation of a lattice of submicro-heterogeneous structure since the atoms inside the submicroscopic "inclusions" and the atoms of the same element of the subsidiary subgroup, but in another valence state and inside the main lattice are under the conditions which are quite close to those that are natural for them in the lattices of the corresponding "extreme"** oxides. Thus, the energy of the exchange interaction changes mainly for the atoms forming the boundary surface of the "inclusions" in the main lattice and since they represent a comparatively small fraction and the total energy of the exchange interaction is comparatively small, this phenomenon will not produce a noticeable heat effect in the formation of a lattice with a submicro-heterogeneous structure from two "extreme" oxides. The energy of the electrostatic interaction of atoms forming the submicroscopic inclusion with all the other particles of the lattice will be different from the lattice of the oxide corresponding only to that valence state of the metal atoms in which these atoms occur in the submicroscopic inclusion. However, this energy also changes for particles forming the main lattice, when the sign of the change will apparently be the opposite. It can be assumed with high probability that the total effect will be quite small in absolute value. Thus, a lattice with a submicro-heterogeneous structure must be formed with a very small heat effect (it probably does not exceed tenths of a kilocalorie). Of course, for this there must be some correspondence of the structures of the "extreme" oxides. Some sort of quantitative calculations of the change in enthalpy in the formation of the lattice of MeO_{1+x} of submicro-heterogeneous structure from $MeO_{1.00}$ and $MeO_{1.50}$ is hardly possible here with sufficient accuracy.



Composition dependence of enthalpy of formation of vanadium oxides.

In the composition range $VO_{1.00}$-$VO_{0.86}$ ($VO_{0.86}$ is the lower limit of homogeneity of vanadous oxide) the enthalpy of formation is also a linear function of composition but the slope here is different from that of the line corresponding to the range $VO_{1.00}$-$VO_{1.27}$ (figure). In other words, at the point of the stoichiometric composition ($VO_{1.00}$) the form of the dependence of the enthalpy of formation on composition changes, which gives grounds for considering that vanadous oxide consists of two phases, which join at the point of stoichiometric composition (the same was said previously for titanous oxide [1]). This is in agreement with the general ideas put forward by A. V. Storonkin [8, 9].

SUMMARY

1. The composition dependence of the enthalpy of formation of vanadium oxides over the range $VO_{0.80}$-$VO_{1.51}$ was established.

2. It was established that the rule for the change in enthalpy of formation of vanadous oxide with composition is similar to that which is found for titanous oxide. This rule does not contradict the idea on the submicro-heterogeneous structure of the lattices of certain oxides of variable composition.

* An MeO_{1+x} lattice in which the Me^{III} atoms are mainly in the form of accumulations and not distributed in the lattice in an isolated state.

** For VO_{1+x} these "extreme" oxides will be $VO_{1.00}$ and $VO_{1.50}$.

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METHOD AND RULES OF FORMATION OF AN EQUILIBRIUM OF FOUR LIQUID PHASES IN CONDENSED FOUR-COMPONENT SYSTEMS

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Until now there have been no systematic investigations in the field of liquid phase equilibrium in four-component systems. Only single papers have been published on two-phase and three-phase liquid states, which however, lay no claims to any kind of generality [1]. Not a single paper is known on four-phase liquid states.

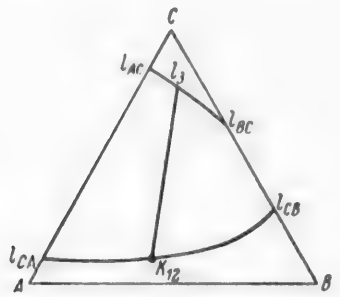

Fig. 1. Formation of a critical node on the layer formation field of a ternary system.

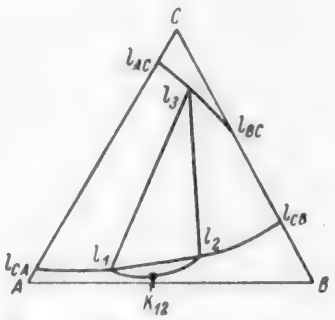

Fig. 2. Formation of a two-phase state region on the phase diagram of a ternary system.

Moreover, a systematic consideration of the problems of equilibrium with a certain number of liquid phases in systems with a different number of components is only possible with a knowledge of the method of formation of the maximum number of liquid phases in a system with a given number of components and the laws of its formation, since an equilibrium with a smaller number of liquid phases can always be genetically related to this state. Evidently a connection must exist between methods of formation of an equilibrium with the maximum number of liquid phases in systems with different numbers of components, since systems with a smaller number of components are the limiting cases in systems with a larger number of components.

Being guided by the latter, we will first consider three-component systems and on the basis of numerous experimental works, we will describe for them the method and rules of formation of a three-phase state.

For three-component systems it was established [2] that the formation of a three-phase liquid state in them is attained only when the homogeneous, single, predominating binary system loses its predominance and this is connected with the occurrence in it of a process of weakening of the interaction between its components, which is reflected by the appearance on the field of the two-phase state of a critical node with a critical point, turned toward the predominating binary system. Let us imagine a ternary system A–B–C (Fig. 1). Let it consist of a binary, homogeneous, predominating system, A–B; the two other systems, A–C and B–C, form layers. Then the initial moment of formation of a three-phase state will consist of the emergence of the critical node l_3K_{12} on the layer formation field ($l_{AC}l_{BC}l_{CB}l_{CA}$) of the ternary system. Subsequently, on continuing the change in

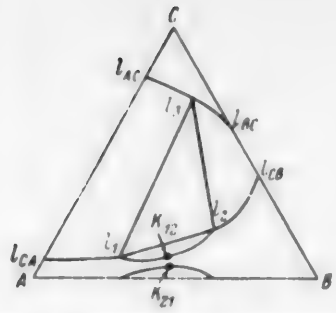

Fig. 3. Formation of two two-phase state regions on the phase diagram of a ternary system.

conditions of state in the required direction, this node develops into a triangle of three liquid phases (Fig. 2), $l_1 l_2 l_3$, with the formation of a new field of two-phase state $l_1 K_{12} l_2$, with a critical point K_{12}, turned toward the binary system A–B. The latter may go right to the line AB and merge with the critical point of this binary system or, without going up to it, merge with the critical point K_{21} (Fig. 3) of a new two-phase state extending inside the composition triangle from the critical point of the binary system A–B. It is not difficult to see that the formation of a three liquid phase state also occurs regardless of whether actual layer formation is observed in the subsidiary binary system B–C or whether it remains homogeneous. In the latter case, however, opposite the line BC there must be the critical point of the two-phase state, extending from the direction of the binary system A–C.

This is the method of formation of a three-phase state in a ternary system. What are the rules of its formation?

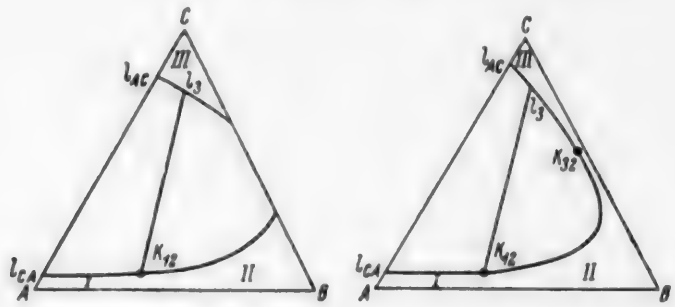

Fig. 4. Critical point on a binodal curve.

First, it should be noted that by the concrete physical conditions of formation of a three-phase state in a ternary system, on the binodal curve there must exist either one or two critical points, i.e., there must be either one pair, I and II, or two pairs, I–II and II–III (with the liquid phase II common to them), of liquid phases with a continuous transition from one to the other. This is illustrated schematically in Fig. 4, where the separate liquid phases are represented by Roman numerals. Hence it follows that the temperature for the beginning of a three-phase state must be higher than the critical temperature of the predominating binary system or (in the more general case) the temperatures of mergence of the critical points of the two fields of layer formation extending toward each other from the predominating system and the three-phase state. In certain cases it may be above the critical temperatures of the two boundary binary systems, which are homogeneous under the conditions of formation of the three-phase state. This rule was established on all the ternary systems with three liquid phases investigated experimentally.

Second, since the formation of three liquid phases proceeds at the node of the region of layer formation with a critical point, turned toward the subsidiary binary system, then the direction of both the critical node and the two sides of the three liquid phase triangle (at least close to the temperature at which the three-phase liquid state occurs), which are also nodes of the same region of layer formation, must be completely determined and unique, obeying the rule of node distribution on the field of the two-phase liquid state. This condition is in agreement with experimental data.

Finally let us note that under certain conditions, the two critical points, by moving along the binodal curve toward each other, may merge with the formation of an invariant, triple critical point (F = 0) with three identical liquid phases. However, such a state is not typical (at the chosen pressure), but even if it exists, nonetheless, not more than three phases can be produced in the system and this number of phases must be considered the maximum possible.

Let us now turn to the problem interesting us. On the basis of the method just mentioned for the formation of an invariant three-phase state in a ternary system, it can be assumed that the same method must exist in a four-component system. Actually, we will consider the quaternary system A–B–C–D, consisting of a single, homogeneous, predominating ternary system A–B–C, which is one of the liquid phases, while the second phase will be its solution in component D. Then the formation of a four-phase state and, moreover, a state with the maximum number of liquid phases must be marked by the appearance in the region of the two-phase state, $l_{AD}l_{BD}l_{CD}l_{DA}l_{DB}l_{DC}$ of a critical node l_4K with a triple critical point* K turned toward the plane of the ternary predominating system A–B–C, indicating a weakening in the interaction of all three of its components with each other (Fig. 5). Such a state would also be invariant (F = 0) and, consequently, not typical of constant pressure conditions. Therefore it must be recognized that in a homogeneous ternary system not all the interrelations of the components are equivalent and that, as a rule, there also exists a predominating interrelation between two of the components, i.e., a predominating binary system is included in the homogeneous ternary system. Let this system be A–B. However, if this is so, with a change in the conditions of the system in the required direction, first of all there will be a weakening in the interrelation of the components in the homogeneous systems A–C and B–C. Geometrically this is reflected in the appearance of critical nodes in the ternary systems A–C–D and B–C–D, respectively, and then in the appearance of three liquid phase triangles and a new two-phase state region with a curve of critical points KK_1, passing directly over plane ABC from face ACD to face BCD (Fig. 6).

Together with this, in the quaternary system there will now exist three phases: phase IV – solutions of components A, B, and C in component D, phase III – solutions of components A, B and D in component C and phase V – solutions of components C and D in mixtures of the binary system A–B. The last two phases, III and V, may pass directly from one into the other if the critical curve KK_1 does not lie on the plane ABC; in the latter case, these phases become isolated.

Since the binary system A–B is the only predominating one in the quaternary system, then the interaction between its components must be reflected geometrically in a definite way both on the two-phase state surface, $l_{AD}l_{BD}l_{CD}l_{DA}l_{DB}l_{DC}$, and on the three-phase state surface, $l_5l_3l_4l'_5l'_3l'_4$. If the interaction in the system A–B is weakened, i.e., the tendency to layer formation arises in it, this also must be reflected.

From Fig. 6 it is easy to establish that the case of equilibrium in the quaternary system is quite analogous to the previously considered case of the layer formation of a predominating binary system, forming part of a ternary system. Thus, if this tendency to layer formation in the predominating system is reflected by the appearance of a critical node, then here one would expect the appearance of not just one, but two critical nodes simultaneously, since the predominating binary system A–B (showing a tendency to layer formation) is simultaneously part of the ternary systems A–B–C and A–B–D. This condition will only be satisfied by two critical nodes Kl_C and Kl_D with the common critical point K_{12} (Fig. 7), formed on the curve $l_5l'_5$ of the three-phase state, corresponding to phase V.

Thus, the tendency to layer formation of the predominating binary system should be reflected geometrically in the initial appearance on the surface of the three-phase state of a critical triangle $l_DK_{12}l_C$. We note that this state (at a given pressure) is invariant, i.e., F = 4 + 1 –4 –1 = 0 (here, as previously, we consider one condition that the two critical phases are identical, reducing the number of degrees of freedom by 1) and consequently, in this respect it is also analogous to a state corresponding to the critical node of the ternary system. Hence, we may arrive at the conclusion that four coexisting liquid phases represent the maximum number of conjugated liquid phases in a quaternary system.

On changing the conditions of existence in the required direction, the critical triangle changes into a tetrahedron, $l_Il_{II}l_{III}l_{IV}$, whose volume corresponds to complexes occurring in a four-phase state (Fig. 8). From the faces of this tetrahedron, $l_Il_{II}l_{IV}$ and $l_Il_{II}l_{III}$, there are formed two new three-phase state spaces, $K_Il_Dl_Il_{II}l_{IV}$ and $K_{II}l_Cl_Il_{II}l_{III}$, ending in the critical nodes K_Il_D and $K_{II}l_C$, extending in the direction of the faces of the composition tetrahedron ABD and ABC. When they separately reach the ternary systems A–B–D and A–B–C, a three-phase state arises, as described previously. The other two faces of the four-phase tetrahedron, $l_Il_{III}l_{IV}$ and $l_{II}l_{III}l_{IV}$, are inside the previously formed three-phase state volume. Adjoining the binodal curves $l_IK_Il_{II}$ and $l_IK_{II}l_{II}$ is a new two liquid phase space with a curve of critical points K_IK_{II} opposite the edge AB of the composition tetrahedron. By moving continuously in this direction and gradually shortening, the curve of

*Three identical phases.

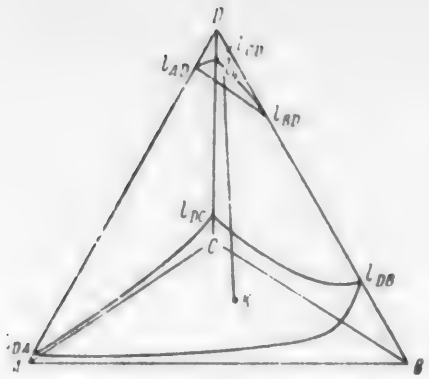

Fig. 5. Appearance of critical nodes on the diagram of a quaternary system.

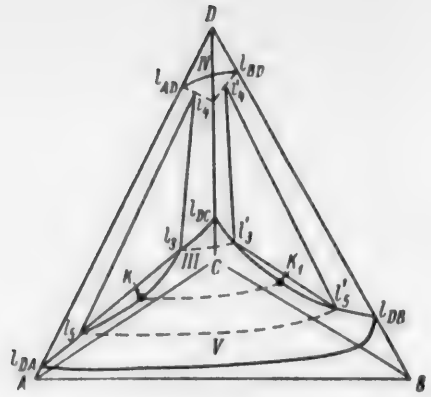

Fig. 6. Formation of liquid phase triangles and a two-phase state region on the phase diagram of a quaternary system.

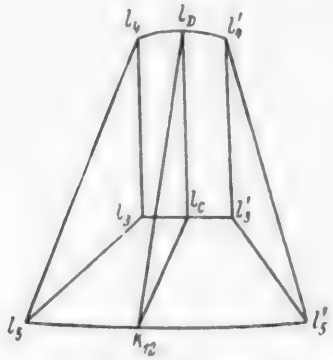

Fig. 7. Appearance of critical nodes and a critical triangle on the three-phase state of a quaternary system.

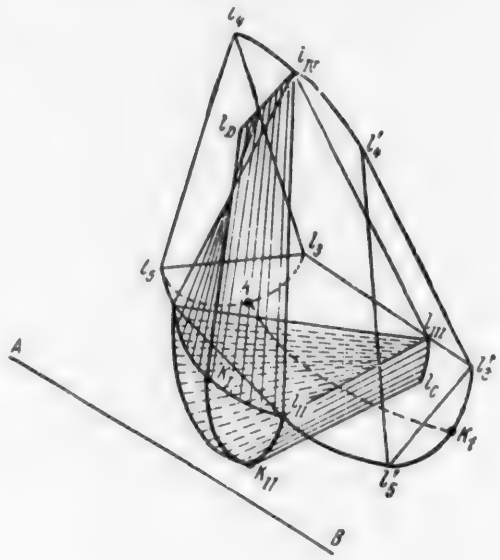

Fig. 8. Formation of a four-phase state tetrahedron.

critical points, in the simplest case, will reach directly to the edge AB and intersect it, merging with the upper critical point of layer formation of this binary system. In more complex cases, beginning at the temperature of the critical point of the binary system A–B, inside the composition tetrahedron there will branch out a third two-phase state volume with its own third curve of critical points. This volume will merge with the two-phase state volume extending toward it, which is connected to the four-phase state, in some common critical point which simultaneously belongs to the second and third critical curves (the second critical curve is opposite the line AB).

From the moment of formation of the critical triangle, the single phase V will consist of two phases, I and II, which pass directly into each other. These phases become isolated either at the temperature of the critical point of the binary system A–B or at the temperature at which both the two-phase state volumes just mentioned merge. It should be also added that the critical node $K_{II}l_C$ may reach the side ABC of the composition tetrahedron only after the curve of critical points KK_1 either wholly or partially successively has reached this face with the formation at it of a binodal curve with a critical point (in the latter case), turned toward BC; in addition, the method described above for the formation of a four-phase space does not involve the necessary presence of a three-phase state in one of the limiting ternary systems which do not contain the predominating binary systems A–B, for example, the system B–C–D. A critical node may be found in the tetrahedron, opposite the face corresponding to such a system.

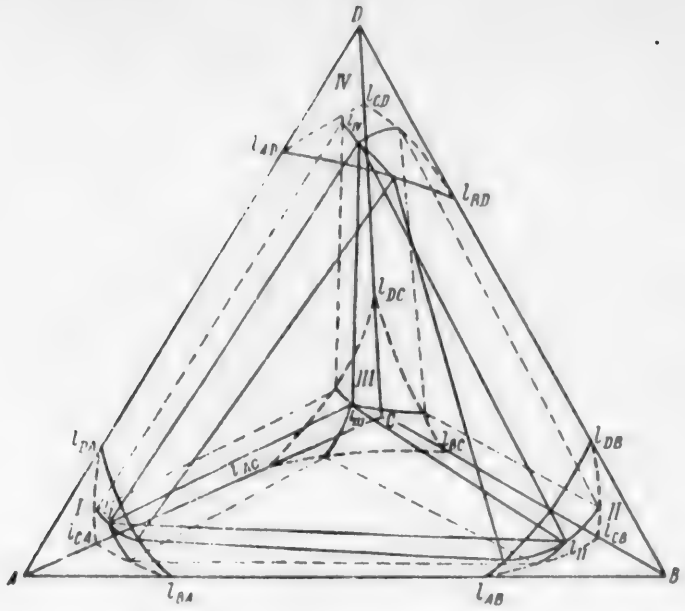

Fig. 9. General appearance of an equilibrium in a quaternary system.

The general form of equilibrium in a quaternary system with the assumption that all three critical nodes extending from the four-phase tetrahedron to the composition tetrahedron faces reach these faces, is given schematically in Fig. 9 and further explanations are not required after what has been said.

Now it is not difficult to establish the rules of formation of a four liquid phase space in a quaternary system. First, from the method of formation of this space it follows directly that the temperature of the beginning of the four-phase state must be above the temperature of the beginning of the three-phase state in at least the two ternary systems which include the binary predominating system. In individual cases, it may be above the temperature of the beginning of the three-phase state in three of the limiting ternary systems. Second, the critical triangle is one of the triangles of the initially, singly existing three-phase state region in the quaternary system. Therefore its direction in the composition tetrahedron and similarly that of the two faces of the four-phase state tetrahedron which are in this volume must be unique and correspond to the rule for the distribution of three-liquid phase triangles in a four-component system with one binary predominating system. The latter undoubtedly will be correct at temperatures close to the temperature of the beginning of the four-phase state.

Until now, only one quaternary system (phenol–water–hexane–sulfur) showing a labile state of four conjugated liquid phases has been investigated. A detailed description of it will be given in a separate paper. Data obtained by studying it demonstrated that the method presented above for the formation of a four-phase space was correct and confirmed the accuracy of the laws deduced. Thus, the temperature of the beginning of the four-phase state in this system corresponds to 95.5-96°, while the temperature for the beginning of a three-phase state in the ternary system water–phenol–hexane is 89°, in the ternary system sulfur–phenol–water, 71°, and in the system sulfur–phenol–hexane, approximately 50°. Thus, as would have been expected, the temperature of the beginning of the four-phase state was found to be above the temperature of the beginning of the three-phase state in the three-limiting ternary systems.

SUMMARY

1. The problem of the method of formation of a four liquid phase state in a quaternary system has been examined.

2. The method of formation of four phases in a quaternary system has been established in connection with the method of formation of a three liquid phase state in a ternary system.

3. It was shown that the temperature at which the formation of a four-phase state begins in a quaternary system must be above the temperature of the beginning of a three-phase state in the two ternary systems including the binary predominating system and, in individual cases, above the temperature of the beginning of formation of a three-phase state in three limiting ternary systems.

4. Close to the temperature of the beginning of the four-phase state, two faces of the four-phase state tetrahedron must have the same direction, corresponding to the rule for the direction of three liquid phase triangles in a quaternary system with one binary predominating system.

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LIQUID – LIQUID EQUILIBRIUM IN THREE-COMPONENT SYSTEMS

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Up to now a large number of papers on the investigation of liquid–liquid equilibria in three-component systems have been published. However, only a small part of these papers is based on a thermodynamic approach. In the majority of cases the empirical laws and characteristics of the liquid–liquid equilibrium diagrams in three-component systems were discussed without using thermodynamics. The present work is an attempt to fill in this gap and to summarize results obtained previously.

Form of Isothermal – Isobaric Curves of Coexistence of Two Liquid Phases of a Ternary System

The hypothesis on the existence of a connection between the form of the coexistence curves of two liquid phases on the concentration diagram of a ternary system and the degree of interaction of the substances making up the system has been put forward more than once in the literature. Does a general thermodynamic relation exist that reflects the existence of such a connection? The differential equation of isothermal–isobaric coexistence of two phases of a ternary system may be considered as such a relation [1].

$$\left(\frac{dx_2}{dx_1}\right)_{\text{coex}\ \ P,\ T} = -\frac{y_1 - y_3}{y_2 - y_3} \qquad (1)$$

In the left section of this equation it is the derivative characterizing the course of the isothermal–isobaric curve on a concentration diagram (x_i is the mole fraction of the i-th component, P the pressure and T the temperature). The right section of Equation (1) includes the values y_i, which are phase effects characterizing the changes in the chemical potentials of the components during the phase process. If a k-phase is formed from a j-phase, then the phase effect of the i-th component in the j-phase is determined in the following way:

$$y_i^{(j)} = \left(\frac{d\mu_i^{(j)}}{dm^{(k)}}\right)_{P,\ T}, \qquad (2)$$

where: $\mu_i^{(j)}$ is the chemical potential of the i-th component in the j-phase and $m^{(k)}$ is the mass of the k-th phase. The phase effects reflect the relation of the chemical potentials to composition, which in its turn characterizes the reaction of the components in the ternary solution.

The values in the left and right sections of Equation (1) may be determined experimentally independently of each other. This important point makes it possible to estimate the reliability of data on solubility from measurements of phase effects. The method of phase effects [1] may be used successfully also in considering the forms of isothermal–isobaric coexistence of liquid phases. One of the problems arising here is that of the possibility of sections on the isothermal–isobaric curve of a liquid–liquid equilibrium bending in toward the homogeneous region. According to thermodynamic theory the isothermal–isobaric coexistence curve must be convex toward the homogeneous region only in the neighborhood of a critical point [2]. Thermodynamics do not limit the forms of the other sections of the binodal. Nonetheless, it has been stated in the literature that the appearance of concave sections on the binodal is due to the presence of impurities which increase the number of components or to

experimental errors [3]. The application of the phase effects method to the study of the triethylamine–phenol–water system [4] has shown this opinion to be incorrect.

Equation (1) may be written in variables of one or other of the coexisting phases. A particular curve corresponds to each of these equations on the composition triangle. When the concentration diagram has a critical point, these curves pass smoothly into each other (Fig. 1). As these curves relate to the same two-phase equilibrium, an interconnection should exist between them which arises from the conditions of equilibrium between the phases.

The "rule of inverse similarity," formulated by Krupatkin [5], is the most general of the empirical rules on the relation between the composition curves of two coexisting phases. According to this rule a line drawn in the concentration triangle parallel to one of the sides and approximately through the middle of the plane limited by the solubility curves divides the layer-formation isotherms into two branches which are similar to each other qualitatively but opposite in curvature and the position of geometric elements. Does this rule have a thermodynamic foundation? The thermodynamic theory requires symmetrical coexistence curves in the neighborhood of a critical point [6]. The axis of symmetry in this case would not be the line drawn parallel to one of the sides of the triangle, but the line drawn through the critical point perpendicular to the tangent of the layer-formation isotherm–isobar. Further from the critical point, the condition of symmetry changes from a quantitative to a qualitative rule. At a distance from the critical point this qualitative rule loses its thermodynamic foundation as it is not based on conditions of equilibrium and stability. Thus, the "rule of inverse similarity" may be considered to have a thermodynamic basis only in a definite region adjacent to a critical point. Outside this region, which depends on peculiarities of the ternary system, one may expect deviations from this rule. Therefore, the experimental data found in the literature which contradict the "rule of inverse similarity" (see for example [3]) may be explained not only as due to experimental inaccuracy, but also to nonfulfillment of this rule.

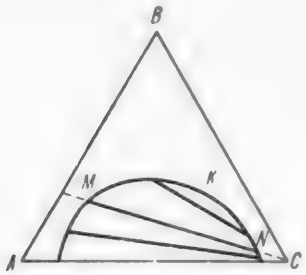

Fig. 1. The position of nodes and coexistence curves on a concentration diagram.

Disposition of Nodes on the Concentration Diagram

The disposition of nodes on a concentration diagram is an important thermodynamic characteristic of a two-phase equilibrium. As with the form of binodals, the disposition of nodes is often connected with the interaction of components. The problem of the disposition of nodes on a concentration diagram is of great practical interest in extraction processes. Therefore a review of the rules related to the disposition of nodes is of considerable value.

D. N. Tarasenkov's rule. The tendency for nodes of a liquid–liquid equilibrium to intersect on a concentration diagram at one point is observed for a whole series of systems [8, 9] and is known as Tarasenkov's rule; it is not a thermodynamic rule and is governed by the peculiarities of the systems. This rule is forbidden by thermodynamic theory only when the vicinity of the critical point is examined. Close to the critical point, the nodes are disposed on the concentration diagram parallel to each other as is demanded by the symmetry requirement of the coexistence curve [6]. The condition of intersection of nodes at one point is incompatible with the condition of symmetry of the coexistence curve in the vicinity of the critical point and the former cannot therefore be fulfilled in this region.

A node coinciding with a secant of the composition triangle.* Among the nodes on the concentration diagram of a liquid–liquid equilibrium there may be one whose direction corresponds with that of one of the secants of the concentration triangle. An examination of such a case is of both theoretical and practical value. From the practical point of view, this case is characterized by the absence of selectivity of solution and the impossibility of extraction if the component added for extraction corresponds to the apex of the triangle toward which this particular node is directed [10].

From the theoretical point of view, in the case when one of the nodes on a composition triangle coincides with the secant from the apex of the i-th component, this corresponds to a transition through the extremum of the

* By secant we mean a line from the apex of the concentration triangle.

chemical potential of the i-th component along the isotherm-isobar of phase coexistence [11, 12]. In Fig. 1 the chemical potential of component C passes through the extremum at points M and N in moving along the binodal. The type of extremum may be determined readily by using the inequality [12]

$$\left(\frac{d\mu_i}{dx_i}\right)_{P, T, \text{sec.}} > 0,$$

where x_i is the gross mole fraction of the i-th component and the derivative is taken by moving in the heterogeneous region along the secant from the apex of the i-th component. This inequality makes it possible to follow the direction in which the chemical potential of the i-th component changes on moving along the isotherm–isobar in the vicinity of the extremum point and, consequently, makes it possible to establish the type of extremum.

Thus, thermodynamic theory leads to the conclusion that a node whose direction coincides with that of a secant from the apex of the i-th component characterizes the state of the i-th component in coexisting phases that corresponds to the extremum of its chemical potential. This state of the i-th component in liquid phases may arise for various reasons.

In conclusion, let us note that the capacity of the node to coincide in direction with a secant does not disappear in changing from molar percents to weight percents.

Solutrope. If one of the nodes is parallel to a side of the concentration triangle, then the content of one of the components will be the same in coexisting phases. Such a state is generally called a solutrope. As the position of the solutrope node and sometimes even the existence of the solutrope depend on the method used for expressing composition, it is necessary to limit oneself beforehand to one of these methods. Evidently, it is preferable to express concentration in mole fractions or percents.

Let us examine the thermodynamic characteristics of a solutrope. Let phases (I) and (II) (Fig. 2) coexist and at some points on the coexistence curve on the composition triangle the content of the second component A_2 is equal in the two phases, i.e.,

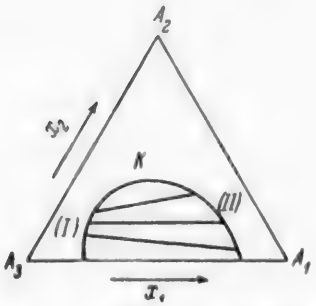

Fig. 2. Disposition of nodes with a solutrope in a ternary system.

$$x_2^{(1)} = x_2^{(2)}. \tag{3}$$

The equation of the isotherm–isobar of phase coexistence, written in form (1) may be readily converted into the following form:

$$\left(\frac{dx_2}{dx_1}\right)_{\text{coex}}{}_{P, T} = -\frac{\zeta_{11}\left(x_1^{(2)} - x_1^{(1)}\right) + \zeta_{12}\left(x_2^{(2)} - x_2^{(1)}\right)}{\zeta_{12}\left(x_1^{(2)} - x_1^{(1)}\right) + \zeta_{22}\left(x_2^{(2)} - x_2^{(1)}\right)}, \tag{4}$$

where ζ is the molar Gibbs potential, $\zeta_{ik}\left(\frac{\partial^2 \zeta}{\partial x_i\, \partial x_k}\right)_{P, T}$, and the superscripts give the numbers of the phases. As with (1), Equation (4) may be related to either of the two coexisting phases. Introducing conditions (3) into Equation (4) we have:

$$\left(\frac{dx_2}{dx_1}\right)_{\text{coex}}{}_{, P, T} = -\frac{\zeta_{11}}{\zeta_{12}}. \tag{5}$$

Equation (5) coincides with the equation for the family of curves of the thermodynamic simplification [13] coming from the apex of the second component. Consequently, one may state that one of the curves of the thermodynamic simplification from the apex of the i-th component touches the binodal at points which correspond to an equal content of the i-th component in the coexisting phases.

What is the physical meaning of Equation (5)? In order to answer this question, let us write (5) in the following way:

$$\zeta_{11}dx_1 + \zeta_{12}dx_2 - \left[d\left(\frac{\partial z}{\partial x_1}\right)\right]_{\text{coex } P,T} = 0. \tag{6}$$

Using the known relation

$$\left(\frac{\partial z}{\partial x_1}\right)_{P,T,x_2} = \mu_1 - \mu_3,$$

we obtain from (6) the condition

$$(d\mu_1)_{\text{coex } P,T} = (d\mu_3)_{\text{coex } P,T} \tag{7}$$

which is the physical meaning of the solutrope phenomenon. On the basis of this condition, the following rule may be formulated: if the contents of one of the components of a ternary system in coexisting phases are the same, then the chemical potentials of the other two components change by equal value on moving along the phase coexistence isotherm–isobar.

An interesting case from the theoretical point of view is a liquid–liquid equilibrium on whose diagram all the nodes are parallel to one of the sides of the composition triangle. If such an equilibrium is characterized by an equilibrium content of the i-th component in the two phases, then the binodal is an envelope for part of the curves of the thermodynamic simplification from the apex of the i-th component and possesses all the properties of these curves.

Position of critical point on binodal. This disposition of nodes on the concentration diagram of a liquid–liquid equilibrium is closely related to the position of the critical point on the binodal. Of special theoretical interest is the case when the critical point is at the apex of the binodal which corresponds to the extremum of the content of one of the components (this case does not require that all the nodes be parallel to one of the triangle's sides). Here thermodynamic examination leads to the following results [2]: if the critical point on the concentration diagram is at the apex of the binodal corresponding to the extremum in the content of the i-th component in a ternary system, then the critical phase corresponding to it is similar thermodynamically to the critical phase of a binary system formed from the ternary one by excluding the i-th component. Such critical phases may be called pseudobinary critical phases.

Alekseev's rule. The statements in the literature [7, 9] on the applicability of V. F. Alekseev's rule to the concentration diagrams of ternary systems have not been justified theoretically up to now. As is known, in the case of binary systems, the line that connects the center of the nodes on a two-phase equilibrium diagram in temperature – composition coordinates is almost a straight line, which justifies extrapolation. However, in the case of concentration diagrams of a liquid–liquid equilibrium in ternary systems, the lines connecting the centers of the nodes are quite curved; therefore extrapolation here requires special justification. This is supplied by thermodynamic theory. Actually, if the coexistence curve is symmetrical in the vicinity of the critical point while the nodes are parallel to each other, then a line drawn through the centers of the nodes should be straight in the vicinity of the critical point. Thus, Alekseev's rule, which he formulated for binary systems, is also applicable in the vicinity of the critical point of a ternary system. According to thermodynamic theory, the curvature of a line drawn through the centers of the nodes decreases as it approaches the critical point. This justifies extrapolation in finding the critical point on the concentration diagram of a liquid–liquid equilibrium.

SUMMARY

1. The problem of the form of the liquid phase coexistence isotherm—isobar in ternary systems was discussed from the point of view of thermodynamic theory.

2. The basic rules and characteristics of the disposition of nodes on the concentration diagram of a liquid–liquid equilibrium in ternary systems was examined. The physical meaning of the phenomenon of solutropy was discussed. The applicability of Alekseev's rule to ternary systems was justified thermodynamically.

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PHYSICOCHEMICAL ANALYSIS OF BINARY SYSTEMS FORMED BY PHENOL WITH CARBAMIDE, ACETAMIDE, AND ACETONE

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It was interesting to study the character of the chemical interaction of phenol with carbamide and also with acetamide and acetone. The last two products should be considered as carbamide in which the amino groups have successively been replaced by one and two methyl radicals. It is known that phenols and amides are compounds characterized by the presence of a hydrogen bond. Therefore, it seemed interesting to determine to what extent a hydrogen bond would appear between unlike molecules, in particular, phenol and carbamide, acetamide and acetone, in the fused state and how this would be reflected in the "composition – property" diagrams. This investigation is also of great practical value in connection with the use of phenol and carbamide in the production of carbamide resins.

TABLE 1

Density, Viscosity and Surface Tension in the Phenol–Carbamide System

C_6H_5OH content of mixt. (mol. %)	d			η			σ		
	80°	90°	95°	80°	90°	95°	80°	90°	95°
95	1.039	1.032	1.029	1.225	0.983	0.858	35.53	33.59	33.02
90	1.047	1.039	1.035	1.344	1.068	0.935	35.87	33.80	33.44
85	1.054	1.046	1.045	1.482	1.177	0.028	36.18	34.39	33.93
80	1.063	1.056	1.053	1.636	1.296	1.115	36.63	34.81	34.31
75	1.069	1.063	1.061	1.799	1.409	1.229	37.01	35.34	34.81
70	1.080	1.071	1.069	1.998	1.552	1.341	37.54	35.91	35.30
65	1.086	1.080	1.077	2.195	1.698	1.462	38.08	36.25	35.95
60	1.095	1.088	1.085	2.415	1.855	1.606	38.71	38.86	36.41
55	—	1.098	1.095	—	—	1.771	—	37.50	36.86

These systems were studied through the density, viscosity, and surface tension. The working procedure was described previously [1-5]. The starting materials were purified: the carbamide by several recrystallizations from water and the phenol, acetamide and acetone by distillation and they had constants close to those presented in the literature [6]. The concentration is expressed in molecular percents, the surface tension in dynes/cm, the viscosity in centipoises, and the density in g/cc.

Phenol–carbamide system (Table 1, Fig. 1). The melting point of this system has already been studied [7, 8]. A compound with the composition $CO(NH_2)_2 \cdot 2C_6H_5OH$ and m.p. 60.6° was detected in the system. The compound was strongly dissociated; the eutectic, corresponding to 33.5 mol. % of carbamide had the same melting point as the compound. This part of the melting point diagram was checked and confirmed [9]. The liquid phase of this system was investigated through the density, viscosity, and electrical conductivity at temperatures of 120 and 135° [9].

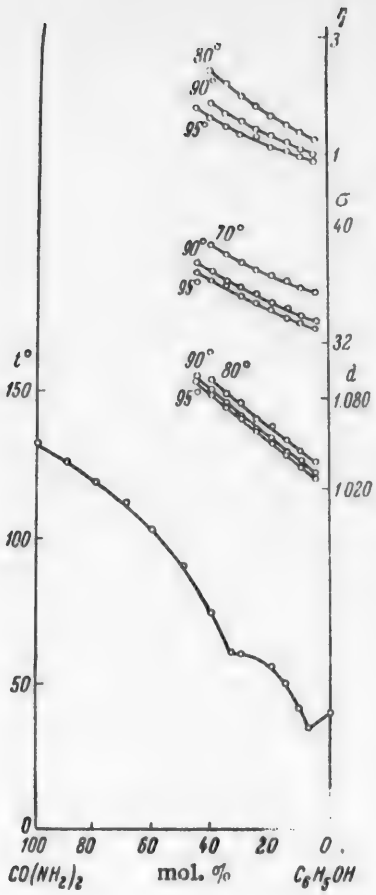

Fig. 1. Melting point curve and density (d), viscosity (η) and surface tension (σ) isotherms in the carbamide–phenol system.

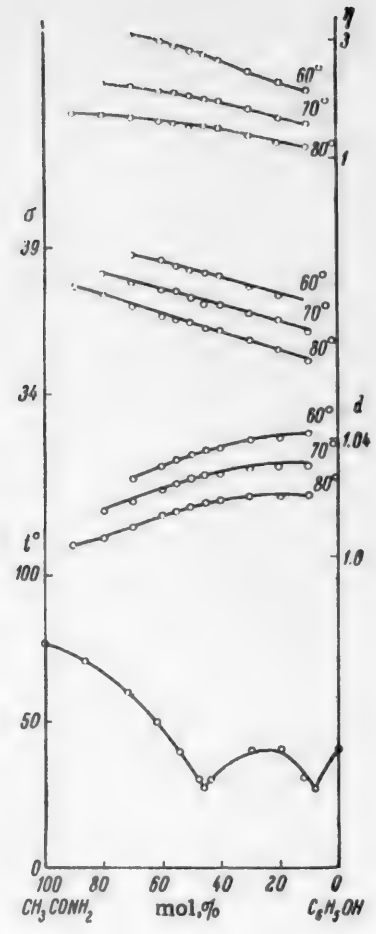

Fig. 2. Melting point curve and density (d), viscosity (η), and surface tension (σ) isotherms in the acetamide–phenol system.

TABLE 2

Density, Viscosity and Surface Tension in the Phenol–Acetamide System

C_6H_5OH content of systems (in mol. %)	d			η			σ		
	60°	70°	80°	60°	70°	80°	60°	70°	80°
10	—	—	1.004	—	—	1.798	—	—	37.73
20	—	1.016	1.006	—	2.292	1.754	—	38.15	37.43
30	1.027	1.019	1.010	3.113	2.244	1.705	38.76	37.83	37.00
40	1.031	0.023	1.014	3.020	2.155	1.654	38.57	37.54	36.67
45	1.033	1.025	1.015	2.913	2.117	1.607	38.38	37.51	36.56
50	1.035	1.027	1.017	2.837	2.074	1.585	38.23	37.26	36.44
55	1.036	1.028	1.018	2.771	2.029	1.564	38.11	37.09	36.25
60	1.037	1.028	1.019	2.682	1.986	1.532	38.04	37.05	36.14
70	1.040	1.030	1.020	2.480	1.813	1.371	37.65	36.73	35.83
80	1.040	1.031	1.020	2.303	1.681	1.282	37.35	36.48	35.53
90	1.042	1.031	1.020	2.135	1.567	1.193	—	36.11	35.12

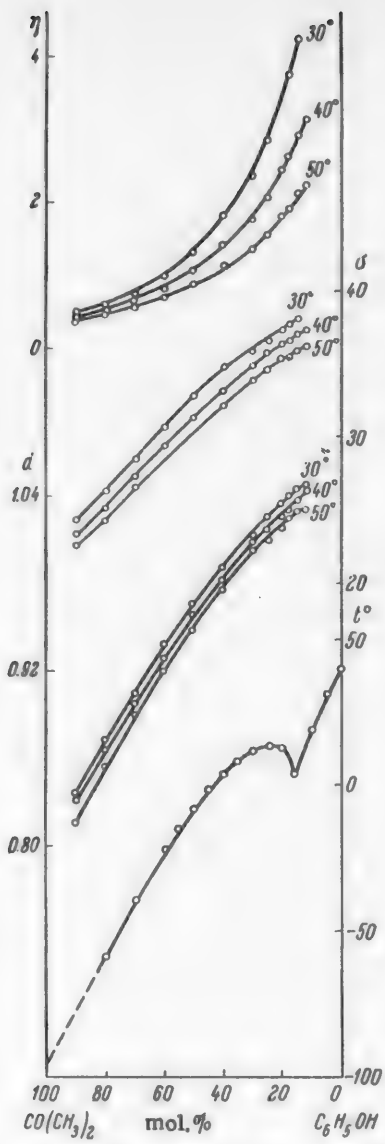

Fig. 3. Melting point curve and density (d), viscosity (η), and surface tension (σ) isotherms in the acetone–phenol system.

The isotherms of these properties did not confirm the presence of a chemical compound in the fused, homogeneous medium. It seemed interesting to plot the density, viscosity, and surface tension curves at lower temperatures. In our work, the density and viscosity were studied at 80, 90 and 95° and the surface tension at 70 and 90°. However, the data obtained also indicated the absence of chemical interaction in the system. The surface tension isotherms increased smoothly from phenol to carbamide. The density and viscosity isotherms changed smoothly and were convex toward the composition axis.

Phenol–acetamide system (Table 2, Fig. 2). The system has already been studied through the melting point [10]; the formation of the compound $2C_6H_5OH \cdot CH_3CONH_2$ with m.p. 40° in it was established. The compound was more stable than in the phenol–carbamide system.

The surface tension isotherms changed by an almost additive line. The curves increased from phenol to acetamide. The density isotherms were curves with slight concavity toward the composition axis and indicated the existence of a compound with the composition $2C_6H_5OH \cdot CH_3CONH_2$. In addition, as Fig. 2 shows, the density in the system decreased from phenol to acetamide. The viscosity isotherms at 60° had an S-form, indicating the presence of a compound in the fused, homogeneous medium; with an increase in temperature, the inflection disappeared and the isotherms changed into curves, which were slightly convex toward the composition axis.

Phenol–acetone system (Table 3, Fig. 3) has been studied through the melting point [11]. As in the first two systems, the presence of a compound with a 2:1 composition, i.e., $2C_6H_5OH \cdot (CH_3)_2CO$, in it was established. The surface tension isotherms at 30, 40 and 50° increased smoothly from acetone to phenol and were slightly concave toward the composition axis. The density isotherms rose steeply from acetone to phenol; they were slightly convex toward the composition axis, which is apparently connected with some chemical interaction in the system in the fused state. The viscosity isotherms were convex toward the composition axis. At first, when phenol was added to acetone, the viscosity increased comparatively slowly and then it increased considerably. Thus, while the viscosity at 30° at 10% phenol was 0.42 centipoise, at 85% phenol it had increased to 4.24 centipoise, i.e., an increase by 10 times was observed. Such a sharp change in the viscosity indicates the presence of chemical interaction between the components in the liquid medium. A comparison of the changes in the viscosity and density isotherms gives grounds for considering that in this system the interaction in the fused, homogeneous medium is less than in the phenol–acetamide system and greater than in the acetone–carbamide system. This is apparently connected with the different values of the dielectric permeability of the components of the systems. High values of the dielectric permeability lead to an increase in the dissociation of the components with the separation of hydrogen ions, which, being good complex-formers, promote the formation of compounds. Thus, the chemical interaction between the components in the melt is stronger the greater their dielectric permeability. In our case, acetamide had the greatest dielectric permeability (59.1); it reacted with phenol best. The dielectric permeability of acetone was less (21.45) and therefore it reacted with phenol more weakly. Chemical interaction in the melt did not appear at all in the carbamide–phenol system.

TABLE 3

Density, Viscosity, and Surface Tension in the Phenol–Acetone System

C_6H_5OH content of mixt. (mol%)	d			η			σ		
	30°	40°	50°	30°	40°	50°	30°	40°	50°
10	0.834	0.831	0.815	0.47	0.42	0.37	24.36	23.26	22.50
20	0.872	0.867	0.855	0.59	0.51	0.45	26.30	25.12	24.20
30	0.904	0.897	0.890	0.74	0.63	0.54	28.54	27.40	26.60
40	0.938	0.928	0.920	0.97	0.80	0.69	30.67	29.53	29.60
50	0.963	0.958	0.948	1.30	1.05	0.87	32.83	31.54	31.40
60	0.990	0.982	0.976	1.83	1.41	1.13	34.69	33.14	32.19
70	1.013	1.009	1.003	2.36	1.76	1.37	35.91	34.92	33.90
80	1.035	1.025	1.018	2.97	2.44	1.81	37.32	36.40	35.34
82	1.040	1.030	1.025	3.75	2.62	1.91	37.70	36.52	35.53
85	1.045	1.037	1.030	4.24	2.91	2.12	38.04	37.01	35.95
87	1.048	1.044	1.031	—	3.15	2.24	—	37.24	36.14

SUMMARY

1. A study was made of the viscosity, density, and surface tension in binary systems formed by phenol with carbamide, acetamide, and acetone.

2. The viscosity and density isotherms confirmed the existence of compounds in the fused, homogeneous medium in the phenol–acetamide and phenol–acetone systems, but did not indicate the presence of compounds in the phenol–carbamide system. The surface tension isotherms did not reflect the presence of a compound in any of the systems studied.

3. It was verified that the stability of the compounds in these systems depended on the value of the dielectric permeability of the component reacting with phenol. According to the stability of the compounds both in the solid phase and in the fused, homogeneous medium, the systems may be arranged in the following order: acetamide–phenol, acetone–phenol, phenol–carbamide.

4. The compounds found in the systems both at the boundary of the two phases and in the homogeneous medium were apparently compounds formed by some type of hydrogen bond.

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** In Russian.

USE OF TWO-SOLVENT METHOD TO STUDY THE FORMATION AND PROPERTIES OF ORGANIC COMPLEXES*

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The proposed two-solvent method, which has a theoretical basis, [1-4] is a method of studying chemical interaction in liquid systems, which also makes it possible to consider the effect of medium. So far there have been few examples of the application of this method to the study of systems in which two complexes are formed. So as to fill this gap, two binary systems (chloral hydrate – antipyrine and pyramidon–salicylic acid), which were previously investigated in the polar solvent, water [5, 6], are examined here in the nonpolar solvent, ligroin.

EXPERIMENTAL

The following reagents were used for the work: pharmaceutical chloral hydrate with m.p. 48°, pharmaceutical antipyrine with m.p. 113°, pharmaceutical pyramidon with m.p. 108°, chemically pure grade salicylic acid with m.p. 155° and a ligroin fraction boiling over the range 120-140°. The advantages and disadvantages of work with ligroin instead of individual hydrocarbons have been pointed out previously [1]. The formation of layers was studied by the visual–polythermal method of V. F. Alekseev [7] in sealed glass ampules in a glycerol thermostat. Crystallization in the pyramidon–ligroin system was studied in the same ampules.

The chloral hydrate – antipyrine – ligroin and pyramidon–salicylic acid – ligroin ternary systems studied contained binary systems characterized by the following data. The chloral hydrate (C) – antipyrine (A) system was described previously [5] and its melting point diagram indicated the presence of two complexes with the composition CA and C_2A. In the ternary system with water, the complex CA was fixed by the solubility minima and the upper triple critical point; the complex C_2A was not reflected on the layer-formation isotherms. The pyramidon (P) – salicylic acid (S) system was investigated through the melting point [6]. Two complexes with the composition PS and PS_3 were formed in it. In the ternary system with water, the complex PS was detected through its homogenizing properties due to its hydrophilicity; the complex PS_3 was hydrophobic and was determined by solubility minima and an upper triple critical point. The antipyrine – ligroin system was studied through its layer formation [1]; the upper critical point of this system was in a high position. The salicylic acid – ligroin system was studied through the melting point [8]. This system was homogeneous in the liquid state. In it the crystallization curve of salicylic acid was S-shaped, which is characteristic of systems that have concealed layer formation [9] or indicates metastable layer formation. The latter was not detected in the system. The chloral hydrate – ligroin and pyramidon – ligroin system were investigated in the present work.

The chloral hydrate – ligroin system was studied through layer formation. The numerical data obtained are given in Table 1; the layer formation curves are shown in Fig. 1, where it is seen that the solubility of ligroin in the chloral hydrate melt depended little on temperature and was equal to 30% on the average, though it first increased slightly with an increase in temperature and then decreased somewhat. On the contrary, the solubility of chloral hydrate in ligroin depended greatly on temperature so that at 50° it was only 7%, but at 130° it was 45%. The upper critical point of the system was not reached.

* Previously published material on the two-solvent method and data on the present article were presented on February 20, 1958 at the All-Union Conference on Methods of Studying Complex Formation in Solutions at Ivanovo.

TABLE 1

Liquid Phase Equilibrium in the Chloral Hydrate – Ligroin System

Ligroin (weight %)	Temperature of layer formation
26.87	127.0°
28.10	119.0
30.00	106.0
30.50	85.0
30.92	66.0
60.09	124.5
70.00	111.0
79.90	94.5
90.00	75.0
93.02	57.0

TABLE 2

Crystallization in the Pyramidon – Ligroin System

Ligroin (weight %)	Crystallization point
0.00	108.0°
10.00	95.0
19.85	91.5
29.91	87.5
40.11	84.0
50.00	81.5
60.08	78.5
69.93	76.5
80.00	73.0
90.00	61.5

The pyramidon – ligroin system was studied through melting point. The data obtained are given in Table 2 and the melting point curve is shown in Fig. 2. It shows that the sloping crystallization curve of pyramidon has an S-shape and occupies almost the whole concentration range of the system. This form of melting point curve indicated that this system either was in a concealed layer forming state or should show metastable layer formation. The latter was not observed on supercooling mixtures of the system to 50°, i.e., an average of 35° below their crystallization point. Thus, this system was a system with concealed layer formation.

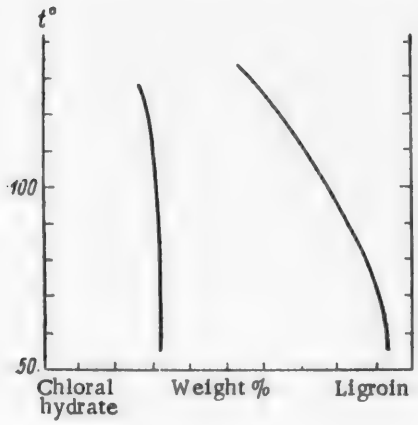

Fig. 1. Liquid phase equilibrium in the chloral hydrate – ligroin system.

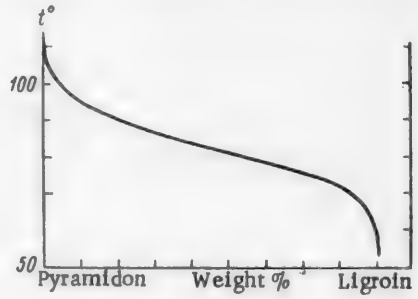

Fig. 2. Crystallization in the pyramidon – ligroin system.

The chloral hydrate – antipyrine – ligroin ternary system was investigated through layer formation. For this purpose we studied six polythermal sections of the ternary system's prism and these passed from the ligroin edge to the face of the chloral hydrate – antipyrine binary system. The sections contained 18, 36.3, 45, 53.3, 70 and 85% of antipyrine. The sections containing 36.3 and 53.3% of antipyrine passed through the compositions of the complexes of the chloral hydrate – antipyrine system. The polytherms of all the sections formed curves close to the ordinate, which rose sharply with an increase in temperature. This indicated the low solubility of the liquid phases of the ternary system and the low temperature dependence of the solubility. The points of complete mixing were high in the sections and were not reached.

Two solubility isotherms in the chloral hydrate – antipyrine – ligroin system were plotted for 100 and 120° from the polytherms obtained and are shown in Fig. 3. The isotherms indicate that the layer formation volume of the ternary system formed with ligroin. As Fig. 3 shows, both complexes of the chloral hydrate – antipyrine system appear on the layer formation isotherms, i.e., in the liquid phase, with complex C_2A appearing as a solubility minimum and complex CA as singular points.

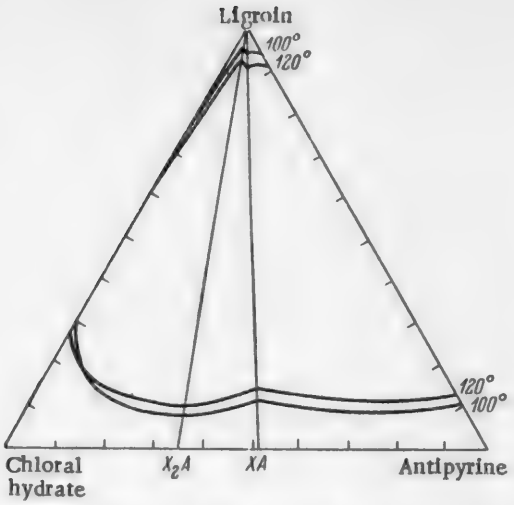

Fig. 3. Solubility isotherms of the chloral hydrate – antipyrine – ligroin ternary system.

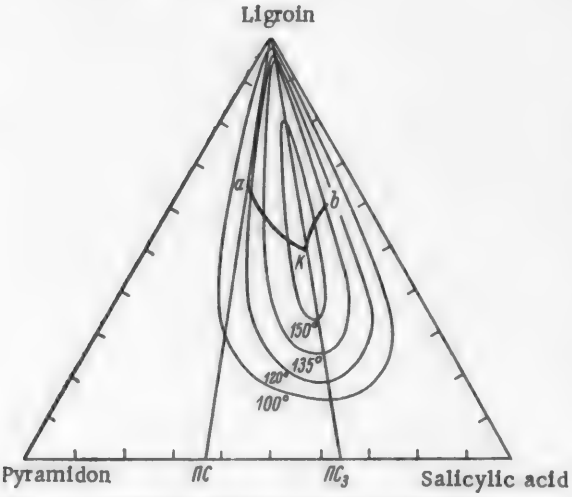

Fig. 4. Solubility isotherms in the pyramidon – salicylic acid – ligroin ternary system. aKb critical line, K upper critical point.

As was stated in [5], in a polar solvent medium (water) only the complex CA was detected in the liquid phase, while the second complex was not reflected on the layer formation isotherms of the ternary system. These facts may be explained by the conjugation rule [4]; this states that in a liquid ternary system the component binary systems are connected to each other by a conjugated effect: an increase in the interaction of one of them results in a weakening in the interaction in the other two binary systems. On the other hand, these facts may be explained by considering the effect of medium on the reacting system. In a ternary system with water, the binary systems have concealed layer formation; at the same time, in the chloral hydrate – water system, the reaction is considerably stronger than in the antipyrine – water system as melting points showed the formation of a heptahydrate between chloral hydrate and water [10]. This created hydration conditions under which the C_2A complex could not attain stability, while the CA complex remained stable and, on the contrary, was stabilized by the hydration processes.

No hydration processes occurred in the nonpolar medium and therefore in the system with ligroin, the layer formation isotherms showed both complexes, even at 120°. The presence of a singular point, i.e., of a qualitatively different (from the solubility minimum in an aqueous solution) geometric element, indicated a qualitatively different method of stabilization of the CA complex in a nonpolar medium by association processes.

The isotherms intersect close to the side of the chloral hydrate – ligroin system. This is connected with the decrease in solubility of ligroin in chloral hydrate at high temperatures.

The pyramidon – salicylic acid – ligroin ternary system was studied through layer formation and by investigating polythermal sections of its prism. We studied seven sections, which passed from the ligroin edge to the face of the pyramidon – salicylic acid binary system and contained 25, 37.4, 45, 54.5, 64.2, 70 and 80% of the acid. The sections with 37.4 and 64.2% of salicylic acid contents passed through the compositions of the complexes of the pyramidon – salicylic acid system. The layer formation polytherms were curves with flat maxima. At the edges of the polytherms the mutual solubility of the liquid phases depended little on temperature and they rose sharply; close to the maximum mixing temperatures the curves were almost horizontal. The maxima of the polytherms from the 1st to the 5th rose and then fell. Consequently, this ternary system had an upper triple critical point. The latter corresponded to 153.5° and had a composition of 50% ligroin, 32% salicylic acid and 18% pyramidon. The triple critical point was in the section corresponding to 64.2% salicylic acid, i.e., in the pyramidon – salicylic acid system it was at the composition of the PS_3 complex, indicating the presence of this complex in the liquid phase. The solubility of ligroin in liquid mixtures of salicylic acid and pyramidon was greater than the solubility of these mixtures in ligroin. Due to this, the layer formation volume was displaced toward the ligroin corner. The left part of the 7th polythermal sections was in the region of metastable layer formation.

From the polytherms obtained, we plotted four solubility isotherms of the pyramidon – salicylic acid – ligroin ternary system at 100, 120, 135 and 150°, which are shown in Fig. 4. The isotherms formed closed curves, decreasing concentrically with an increase in temperature and finally changing into the upper critical point K. All the isotherms had a minimum of mutual solubility of the liquid phases, which lay on the section corresponding to the composition of the PS_3 complex in the pyramidon – salicylic acid binary system. Consequently, these minima and the critical point simultaneously prove the formation of the PS_3 complex and its presence in the liquid phase of both the pyramidon – salicylic acid binary system and of the ternary system.

Figure 4 shows a projection (on the composition triangle) of a line which passes through the maxima of the layer formation polytherms in the form of the curve aKb. It is close to the critical line due to the peculiarities of the positions of the sections. This curve has a discontinuity, which coincides with the upper triple critical point; this confirms the fact found previously [5, 6] that the formation of a chemical compound in the dominating binary system is reflected on the critical line of the layer formation surface of a ternary system.

In the pyramidon – salicylic acid – ligroin ternary system, the region of layer formation arises with all three homogeneous component binary systems. This phenomenon, which was explained previously [5], is connected with the particular conjugated effect between the binary systems of this ternary system and with the systems with concealed layer formation behaving as layer forming systems [9]. Here the binary systems formed with ligroin are close to the layer formation. An increase in the interaction between pyramidon and salicylic acid in the dominating system leads to a weakening of the interaction in the other systems and between the dominating system and ligroin. This process passes from the planes of the binary systems containing ligroin into the prism of the ternary system and causes layer formation between the PS_3 complex and ligroin.

The systems described show that in a polar solvent, water, both complexes of the pyramidon – salicylic acid system, PS and PS_3, were found in the liquid phase and one of the proposed forms for layer formation isotherms in ternary systems with two compounds in the dominating system was established [11]. In a nonpolar solvent, ligroin, only the complex PS_3 was detected, while the complex PS was not indicated by layer formation in the liquid phase. These facts are, on the one hand, closely related to the interaction of the reacting system and its complexes with the medium and, on the other hand, to the conjugated effect of the binary systems in the ternary one. In a system with water, the hydrophilic PS complex was naturally stabilized by hydration processes, while the hydrophobic PS_3 complex was naturally stabilized by hydration processes, while the hydrophobic PS_3 complex was established by solubility minima. In a system with ligroin there are no hydration processes and the hydrophilic complex cannot be stabilized and reflected on the isotherms. The hydrophobic complex remains stable and is detected on the layer formation isotherms.

The example of this system shows the error of the superficial impression that complex formation in organic systems is best studied in nonpolar solvents. It is necessary to use both polar and nonpolar solvents.

The data given show, on the one hand, that the two solvent method is reliable for studying complex formation in organic systems with two complexes. It makes it possible to detect both complexes and to determine their composition and a series of properties. On the other hand, these data reflect the effect of medium on chemical interaction in a system, on the stability, dissociation and other properties of the complexes forming it and lead to the following conclusion: if two complexes are formed in a binary system, then in a liquid phase with a solvent, the more stable of these will be the complex containing the greatest amount of that component of the reacting system which reacts least with the third component, namely, the solvent.

Presumably this conclusion can be extended so that in the case when several complexes are formed in a system, these may be arranged in order of increasing stability according to their increasing content of the component which reacts least with the solvent. The latter interaction is readily determined by the form of the phase diagram of binary systems formed with the solvent. This conclusion may be extended to cover multicomponent systems with binary and ternary compounds. The two solvent method makes it possible to test this conclusion experimentally.

SUMMARY

1. The chloral hydrate – ligroin system was studied through layer formation. It was found to be a system with an upper critical point. The pyramidon – ligroin system was studied through the melting point; it was shown to be a system with concealed layer formation.

2. The chloral hydrate – antipyrine – ligroin ternary system was studied through layer formation. Its layer formation isotherms show two complexes of the dominating system.

3. The pyramidon–salicylic acid – ligroin ternary system was studied through layer formation. Its layer formation isotherms reflect one complex of the dominating system in solubility minima, an upper critical point and a discontinuity in the critical line. In the given ternary system, a layer formation region arises with all three homogeneous component binary systems. This phenomenon was explained.

4. It was shown that the two solvent method is reliable for studying complex formation in organic systems with two complexes. It makes it possible to detect all of the complexes in the system and to determine their composition and a series of properties. It was thus shown that the most stable of two complexes is the one containing the greatest amount of that component of the reacting system, which reacts least with the third component, namely, the solvent.

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INTERACTION BETWEEN GALLIUM NITRATE AND STILBAZO IN AQUEOUS SOLUTIONS

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According to literature data [1], gallium (III) reacts with stilbazo [stilbene-4,4'-bis(azo-1)3,4-dihydroxybenzene-2,2'-disulfonic acid] in a weakly acid medium to form violet or red-violet solutions. Stilbazo interacts with a series of other elements, but only the reactions with aluminum [1, 2], tin [3] and tungstate [4, 5] have been investigated. In the present article we report some results of a photometric investigation of the interaction between solutions of gallium (III) nitrate and stilbazo.

Preliminary Tests

A starting 0.1 M solution of gallium nitrate was prepared by solution of metallic gallium (99.99% Ga) in nitric acid. A preparation of the diammonium salt of stilbazo was purified and converted into the acid as described previously [4].

When dilute solutions of the reagents were mixed, the mixtures had a blue-violet color at pH 2-3 or a bright red color at pH 4-6.5. Concentrations of the order of 10^{-4} M gave a color which was stable for several hours. A precipitate was formed on longer storage. With higher concentrations, a precipitate formed immediately after mixing. The gallium-stilbazo compound floated at a water—benzene boundary. Aqueous solutions of the gallium-stilbazo compound apparently were colloidal.

Dependence of optical density of solutions on wavelength, pH, and interaction time. The spectral characteristics of mixtures of gallium nitrate and stilbazo solutions with excess gallium and different pH values are shown in Fig. 1. The optical density was measured 10-15 minutes after the addition of nitric acid or sodium hydroxide to the solution mixtures for pH adjustment. The spectral characteristics of pure stilbazo solutions were almost independent of acidity in the pH range from 1.5 to 6.5.

The curves in Fig. 1 and the results of measuring the optical density at other pH values, which are not presented in the figure, undoubtedly indicate the formation of not less than two compounds: a blue-violet one in the pH region from 2 to 3 with a maximum at 550 mμ and a red one at higher pH values with a maximum at 495 mμ.

The pH dependence of optical density at λ 495 and 550 mμ is illustrated in Fig. 2. The course of the curves shows that the blue-violet compound is not formed at all at pH < 2 and at pH of about 3 and above destruction begins, coupled with the formation of the red compound.

The maximum optical density value of the blue violet solutions was reached after 8-10 minutes; it remained constant for several hours and then began to decrease due to precipitation of the gallium-stilbazo compound. The maximum optical density value of the red solutions at pH > 4 was reached immediately after mixing of the solutions and remained constant for a period of days.

Composition of gallium-stilbazo compounds. The composition of the gallium-stilbazo compounds in solutions was determined by the isomolar series method at pH values of 2.7, 3.5 and 5.8. The total concentration of gallium and stilbazo in solutions of the first and second series (pH 2.7 and 3.5) was $8 \cdot 10^{-5}$ M and in solutions of the third series (pH 5.8), $6 \cdot 10^{-5}$ M. The results obtained are illustrated by Figs. 3 and 4. From these data it is readily seen

Fig. 1. Spectral characteristics of mixtures of gallium nitrate and stilbazo solutions at various pH values. Concentration of gallium nitrate $2 \cdot 10^{-3}$ M and of stilbazo $1.2 \cdot 10^{-5}$ M. SF-4 spectrophotometer with a 1.004 cm cell. pH values: 1) 2.1; 2) 3.3; 3) 6.6; 4) pure stilbazo solution (pH 2).

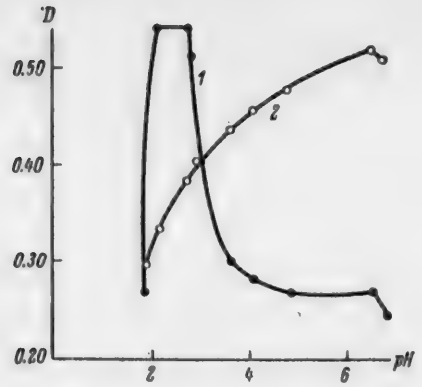

Fig. 2. pH dependency of optical density of mixtures of gallium nitrate and stilbazo solutions at 550 mμ (1) and 495 mμ (2). Concentration of gallium nitrate $2 \cdot 10^{-3}$ M and of stilbazo $1.2 \cdot 10^{-5}$ M. SF-4 spectrophotometer with 1.004 cm cell.

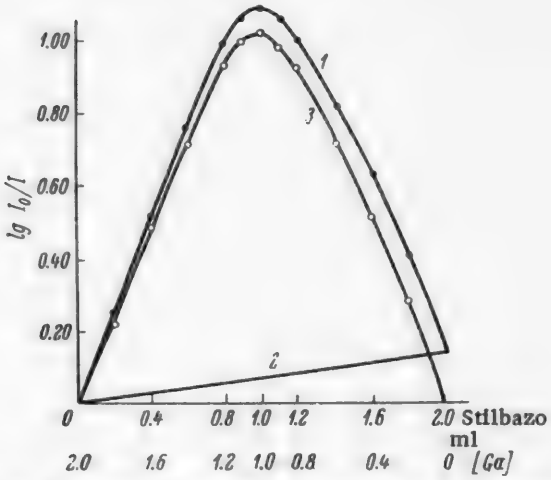

Fig. 3. Isomolar series of mixtures of gallium nitrate and stilbazo solutions at pH 2.7. Blue-violet solutions. 1) Change in optical density in isomolar series, 2) in pure stilbazo solutions, 3) deviation from additivity. FM photometer, M-57 light filter and 1.00 cm cell.

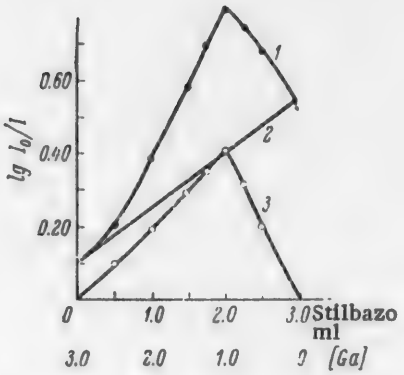

Fig. 4. Isomolar series of mixtures of gallium nitrate and stilbazo solutions at pH 5.8. Red solutions. 1) Change in optical density in isomolar series, 2) in pure stilbazo solutions, 3) deviation from additivity. M-50 light filter, 1.00 cm cell.

that at pH 2.7, that is in the pH interval from 2 to 3, a blue-violet compound is formed in which gallium and stilbazo are present in a ratio of 1:1 (Fig. 3); at pH 5.8 (and consequently, in the pH interval from 4 to 6.6) a red compound is formed in which gallium and stilbazo are present in the ratio 1:2 (Fig. 4).

At pH 3.5, the maximum on the composition – property curve was indistinct and occurred within the limits of gallium : stilbazo ratios of 1:1 and 1:1.5. At this acidity, the solutions apparently contained a mixture of the blue-violet and red compounds. It can be assumed that the interaction between gallium nitrate and stilbazo proceeds according to the following schemes.

At pH 2-3:

$$Ga(NO_3)_3 + (HO)_4R = GaO_2R(OH)_2(NO_3) + 2HNO_3;$$

at pH > 3:

$$Ga(NO_3)_3 + 2(HO)_4R = Ga[O_2R(OH)_2][OR(OH)_3] + 3HNO_3,$$

where $R(OH)_4$ is a stilbazo molecule.

Solubility of gallium-stilbazo compounds. As noted above, certain properties of the gallium-stilbazo solutions indicate that they have a colloidal character.

From the dependence of the optical density of the solutions on the concentration of the components, it is possible to calculate the solubility of the gallium-stilbazo compounds.

Table 1 shows measurements of the optical density at 20° and pH 2.7 and 5.7 in relation to the gallium nitrate concentration. The stilbazo concentration was $2 \cdot 10^{-5}$ M in all the mixtures. The optical density of the blue-violet solutions (pH 2.7) was measured at λ= 550 mμ on an SF-4 spectrophotometer with a cell with a layer thickness of 1.005 cm; for the red solutions (pH 5.7) we used an FM photometer with a light filter with an effective wavelength of 496 mμ and a cell with a layer thickness of 1.00 cm.

The data in Table 1 show that the maximum value of the optical density of blue-violet solutions was attained only with more than 25 times the equivalent excess of gallium nitrate and of red solutions, with only 6-8 fold excess. Apparently the solubility of the red compound was less than that of the blue-violet one.

TABLE 1

Dependence of Optical Density of Gallium-Stilbazo Solutions on the Concentration of Gallium Nitrate (stilbazo concentration $2 \cdot 10^{-5}$ M, temperature 20°)

Gallium concentration ($M \cdot 10^5$)	lg I_0/I	
	pH 2.7	pH 5.7
	0.03	0.16
0.5	—	0.32
1.0	0.18	0.36
1.5	0.26	—
2.0	0.32	0.41
3.0	0.41	0.44
4.0	0.48	0.47
5.0	0.53	—
6.0	0.55	0.49
8.0	0.58	0.50
10.0	0.60	0.50
14.0	0.64	—
20.0	0.69	0.50
30.0	0.72	—
40.0	0.74	—
50.0	0.76	—
100.0	0.80	—
200.0	0.80	—

TABLE 2

Solubility* at 20° of Blue-Violet (at pH 2.7) and Red (at pH 5.7) Gallium-Stilbazo Compounds (Stilbazo Concentration $2 \cdot 10^{-5}$ M)

Total $Ga(NO_3)_3$ concentration ($M \cdot 10^5$)	pH 2.7		pH 5-7	
	amt. of blue-violet comp. ($M \cdot 10^5$)	solubility (mole/liter $\cdot 10^5$)	amt. of red compound ($M \cdot 10^5$)	solubility (mole/liter $\cdot 10^5$)
1.0	0.31	0.69	0.60	0.40
1.5	0.54	0.96	—	—
2.0	0.71	1.29	0.75	0.25
3.0	0.96	1.04	0.84	0.16
4.0	1.15	0.85	0.93	0.07
5.0	1.29	0.71	—	—
6.0	1.34	0.66	0.99	0.01
8.0	1.43	0.57	—	—
10.0	1.49	0.51	—	—
14.0	1.60	0.40	—	—
20.0	1.74	0.26	—	—
30.0	1.83	0.17	—	—
40.0	1.88	0.12	—	—
50.0	1.94	0.06	—	—

*Calculated from data in Table 1.

To calculate the solubility it is necessary to know the equilibrium concentrations of one of the components: with excess stilbazo, the equilibrium concentrations of gallium and with excess gallium, the equilibrium concentrations of stilbazo. To determine these concentrations, it is necessary to calculate the amount of gallium-stilbazo compound formed at given total concentrations of gallium nitrate and stilbazo. The calculations were carried out according to the formula derived for the case when two out of three components in a heterogeneous equilibrium are colored [6].

The amount of blue-violet compound was calculated from the formula

$$[GaO_2(OH)_2R \cdot NO_3] = \frac{[GaO_2(OH)_2R \cdot NO_3]_M (D - [R(OH)_4]_0 a_M l)}{D_{max} - [GaO_2(OH)_2R \cdot NO_3]_M a_M l},$$

and the red, from the formula:

$$[GaO_3(OH)_5R_2] = \frac{[GaO_3(OH)_5R_2]_M (D - [R(OH)_4]_0 a_M l)}{D_{max} - 2[GaO_3(OH)_5R_2]_M a_M l}.$$

$[R(OH)_4]$ is the total stilbazo concentration, equal to $2 \cdot 10^{-5}$ M; D is the observed value of the optical density at a given total gallium nitrate concentration ($\log I_0/I$ is given in Table 1); D_{max} is the maximum value of the optical density attained with a sufficient excess of gallium nitrate for all the stilbazo to be bound in the gallium-stilbazo compound (given in Table 1). $[GaO_2(OH)_2R \cdot NO_3]_M$ and $[GaO_3(OH)_5R_2]_M$ are the amount of blue-violet and red compounds at D_{max} and equaled $2 \cdot 10^{-5}$ and $1 \cdot 10^{-5}$ M, respectively; a_M is the molar extinction coefficient of stilbazo, equal to 3400 at pH 2.7 and λ = 550 mμ and 8000 at pH 5.7 and λ = 500 mμ; l is the layer thickness of the cell in centimeters.

The equilibrium concentrations of gallium and stilbazo (and consequently, the solubility of the gallium-stilbazo compounds) were then calculated as the difference between the total concentration of gallium nitrate or stilbazo and the amount of gallium-stilbazo compound formed at the given total concentration of gallium nitrate. The results are presented in Table 2.

Thus, the solubility at equivalent total concentrations of gallium nitrate and stilbazo equaled $1.29 \cdot 10^{-5}$ mole/liter (at pH 2.7) for the blue-violet compound and $0.40 \cdot 10^{-5}$ mole/liter (at pH 5.7) for the red compound. The data refer to 20°. The corresponding values of the solubility product are $1.7 \cdot 10^{-10}$ and $2.6 \cdot 10^{-16}$. The results presented may be used for investigating the interaction between gallium nitrate and addends which form colorless compounds with gallium (for example, fluorine ions). The decrease in the optical density of a solution of the gallium-stilbazo compound when the addend solution was added would thus serve as a measure of complex-formation.

SUMMARY

1. The interaction between gallium nitrate and stilbazo in aqueous solutions at stilbazo concentrations of 10^{-5}–10^{-4} M and gallium nitrate concentrations of 10^{-5}–10^{-3} M was investigated photometrically.

2. The interaction produced colloidal solutions, blue-violet in the pH range from 2 to 3 and red at pH 4 to 6.5. In the pH range from 3 to 4, the solutions had a mixed color. The light absorption maximum of the blue-violet solutions was at 550 mμ and of red solutions, at 495 mμ.

3. Gallium and stilbazo were present in the blue-violet compound in a 1:1 ratio. It was assumed that this compound corresponded to the formula $Ga[O_2(OH)_2R]NO_3$. Gallium and stilbazo were present in the red compound in the ratio of 1:2. It was assumed that the composition of the compound corresponded to the formula $Ga[O_2(OH)_2R][O(OH)_3R]$.

4. The solubility of the gallium-stilbazo compounds was determined. At 20° and equivalent total concentrations of gallium nitrate and stilbazo, the solubility of the blue-violet compound equaled $1.3 \cdot 10^{-5}$ mole/liter and the solubility product was $1.7 \cdot 10^{-10}$, while for the red compound, the solubility was $0.4 \cdot 10^{-5}$ mole/liter and the solubility, $2.6 \cdot 10^{-16}$.

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ISOTOPIC EXCHANGE OF SULFUR ATOMS OF 2-MERCAPTOBENZTHIAZOLE AND ELEMENTARY SULFUR IN THE PRESENCE OF CARBON BLACKS

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As is known, carbon blacks (lamp black, chimney soot, channel black etc.) are important components of rubber mixtures on which high physicomechanical properties of rubbers (strength, wear-resistance, hardness etc.) depend. Experimental data of recent years [1-4] now makes it possible to consider that functional groups (oxygen–hydrogen containing compounds and double bonds of aromatic rings forming part of the structure of the blacks,etc.) in the structure of blacks are active centers for chemical interaction of the blacks with both rubber and other ingredients of the rubber mixtures. In the work of Studebaker [5] and Dogadkin et al. [6], the interaction of sulfur with blacks was demonstrated and in the work of Blokh [7, 8], radioactive sulfur and accelerators were used to establish that carbon black reacted chemically not only with sulfur, but with mercaptobenzthiazole and tetramethylthiuramide sulfide. Lezhnev and Kuz'minskii [9] also observed chemical interaction of gas black with the antioxidant phenyl-β-naphthylamine. In the interesting work of Dogadkin, Skorodumova and Kovaleva [10] it was established that blacks with a lower oxygen content bound a larger amount of sulfur per unit of surface (channel black was an exception). As was shown in this work, sulfur reacted mainly with active parts of the black surface not occupied by oxygen groups, which were olefinic double bonds of surface hexacarbonium groupings in the surface of the black structure, forming sulfide compounds in which the sulfur was nonlabile. The activation energy for the addition of sulfur to black was approximately 15 kcal/mole.

In our previously published work [11], it was shown by means of radioactive isotopes that during the vulcanization of rubber, exchange of sulfur atoms occurred between the accelerator and the vulcanizing substances and the intensity of this characterized the activity of the accelerator. It was established that the separate components of the rubber mixture had an essential effect on the exchange of sulfur atoms. Thus, for example, in the presence of amino compounds (diphenylguanidine, triethylamine etc.) there was more intense isotopic exchange of sulfur atoms [12], while in the presence of zinc oxide, a certain fall in isotopic exchange was observed [13]. It was important to determine the effect of carbon blacks present in the rubber mixture on the isotopic exchange of sulfur. As is known, different types of black differ from each other in specific surface, adsorptive capacity, pH,and presence and character of functionally active groups. Undoubtedly all this is of great importance in the characteristics of the strengthening properties of the blacks. Thus, for example, the specific surface of channel black (90-100 m^2/g) and imported black of grade "Filblack-0" (80-90 m^2/g) is 4-5 times greater than the specific surface of lampblack (19-29 m^2/g). Channel black has pH 3.52, while chimney soot has pH 8.06. The adsorption of diphenylguanidine in percents for channel black is 16.16% and for "Filblack-0", 5.62%. In the light of contemporary ideas, the vulcanization process may be considered as a radical process. In the work of Bresler et al. [14] and Blokh [15], by means of electron paramagnetic resonance, paramagnetic spectra were observed during the vulcanization of natural rubber with tetramethylthiuramide sulfide.

We consider that on the enormous surface of the black structures, interaction occurs between adsorbed accelerators and sulfur with the formation of unstable polysulfide compounds and on decomposition of these, isotopic exchange of sulfur atoms occurs. The active fragments of sulfur thus liberated interact both with the black and with the film of rubber oriented on the surface of the black to form a vulcanization structural lattice. On the surface of the black structure, oxidation-reduction reactions may occur which are sources of free radicals

and, as was shown by Dolgoplosk and Tinyakova, these may cause processes leading to both structuralization and destruction of polymer chains [16].

EXPERIMENTAL

A study was made of the isotope exchange of sulfur atoms of 2-mercaptobenzthiazole and elementary sulfur in the presence of lamp and channel blacks and the highly disperse, strengthening chimney soot ("Filblack-0"), taken in various ratios to the sulfur – 5:1, 10:1 and 20:1. The ratio of sulfur to mercaptobenzthiazole (Captax) was 1:0.5 in all experiments. All experiments were carried out in sealed ampoules in xylene with molding rubber at 135° for various times (from 15 to 240 minutes). The greatest experimental difficulty was the isolation of mercaptobenzthiazole from the reaction system in which channel black or chimney soot was present in large amounts, since during heating, the accelerator, Captax, was bound (by chemisorption also) in large amounts by the active centers of the blacks. The procedure for isolating mercaptobenzthiazole after being heated with black and sulfur consisted of treatment of the system with 0.5% sodium hydroxide, i.e., conversion of the mercaptobenzthiazole into the water-soluble sodium salt, which was separated from the sulfur and black by subsequent precipitation of the mercaptobenzthiazole with concentrated hydrochloric acid. The mercaptobenzthiazole isolated was purified by recrystallization and dried to constant weight, when it had m.p. 176-178°. The radioactivity of the mercaptobenzthiazole isolated was determined and the percent isotopic exchange calculated by the generally accepted procedure [17].

The experimental data are presented in Figs. 1-3.

An examination of the experimental data shows that the isotopic exchange of sulfur atoms of 2-mercaptobenzthiazole and elementary sulfur in the presence of all types of black studied in this work proceeds more rapidly than in the absence of blacks. As can be seen from the kinetic curves presented, isotopic exchange of sulfur atoms during heating at 135° for 240 minutes was approximately 35-37% in the absence of blacks, while with lampblack and chimney soot, the isotopic exchange reached 80-100% (Fig. 2).

The effect of the quantitative black content of the reaction system on the isotopic exchange appeared especially in the case of channel black, which has pH 3.52. With a channel black to sulfur ratio of 5:1, the exchange of sulfur atoms after 2 hours' heating was 60-65%. An increase in the channel black content until the ratio to sulfur was quadrupled (20:1) led to a strong fall in the isotopic exchange of sulfur atoms (to 20-30%). These data should apparently be explained by both the acid reaction of the medium (pH 3.52), which has a decelerating action on rubber vulcanization processes, and the irreversible chemical binding of sulfur and mercaptobenzthiazole by the functional groups of the black structure. Thus, an analogy was observed between the reduction in the rate of isotopic exchange and the deceleration of the vulcanization process in an acid medium produced by channel black.

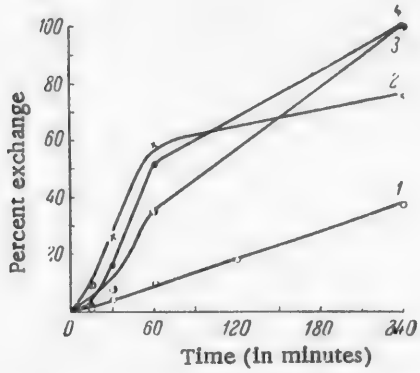

Fig. 1. Isotopic exchange of sulfur atoms in the presence of blacks at 135°. Ratio [S]: [Captax]: [black] = 1:0.5:5. 1) Without black (control experiment); 2) lampblack; 3) chimney soot; 4) gas black.

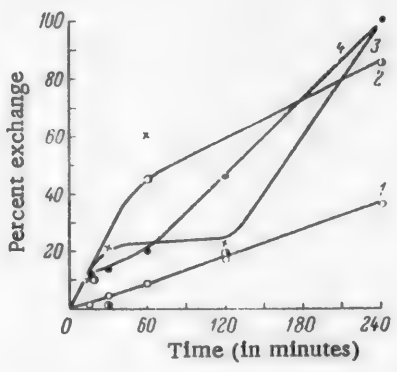

Fig. 2. Isotopic exchange of sulfur atoms in the presence of blacks at 135°. Ratio [S]: [Captax]: [black] = 1:0.5:10. Notation as in Fig. 1.

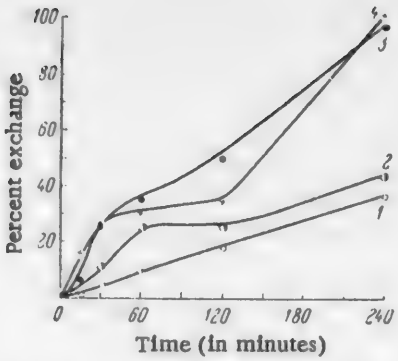

Fig. 3. Isotopic exchange of sulfur atoms in the presence of blacks at 135°. Ratio [S]:[Captax]:[blacks] = 1:0.5:20. 1) Without black; 2) gas black; 3) chimney soot; 4) lampblack.

A different picture was observed in the case of chimney soot. Chimney soot, which has pH 8.06, accelerates the vulcanization process and, as can be seen from the data in Fig. 3, at concentrations of black close to technological levels, isotopic exchange proceeds most rapidly in the presence of chimney soot "Filblack-0." From technological practice it is known that in all the main properties, the highly disperse chimney soot from liquid fuel surpasses blacks of the acid type [18]. In the presence of lampblacks, which have the minimal content of active functional groups, the isotopic exchange of sulfur atoms also proceeds with a great rate.

Thus, the data obtained show that in the process of rubber vulcanization, isotopic exchange of sulfur atoms proceeds at a greater rate in the presence of blacks.

SUMMARY

1. A study was made of the isotopic exchange of sulfur atoms of 2-mercaptobenzthiazole and elementary sulfur in the presence of lampblack, chimney soot and channel black at 135°.

2. It was established that the isotopic exchange of sulfur atoms proceeded at a greater rate in the presence of all the types of black studied than in the absence of blacks.

3. It was shown that when the exchange reactions were carried out in the presence of channel black, taken in the amounts used in rubbers, there was a fall in the isotopic exchange of sulfur atoms in comparison with the exchange occurring in the presence of lampblack and chimney soot.

4. It was established that there was an analogy between the effect of blacks on the rate of the vulcanization process and the isotopic exchange of sulfur atoms.

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DEPENDENCE OF THE DISTRIBUTION OF PLATINUM IN IMPREGNATED Pt – C CATALYST ON THE CONCENTRATION OF THE ORIGINAL H_2PtCl_6 SOLUTION AND THE CHARACTER OF THE CARBON GRANULATION

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We previously [1] used an x-ray method to determine the distribution of platinum through the depth of the grain of a platinized charcoal catalyst with various grain sizes of the charcoal. This catalyst was prepared similarly to the one described below. The experiments were carried out with only one platinum concentration and the x-ray determinations were not particularly accurate since they were carried out on a normal x-ray apparatus, where accurate determination of the radiation was impossible. In addition, accurate measurement of the blackening intensity on the photographs was prevented by the fibrous structure of the charcoal, which was noted in the given work. It was necessary to eliminate either this obstacle or the need for microphotometry. In connection with this, we rejected the photoregistration method and decided to repeat the experiments under strictly comparable conditions on an ionization x-ray apparatus for structural analysis, URS-50-I, fitted with a Geiger-Müller counter, a time relay and appropriate recording equipment. Under these conditions, the fibrous structure of the charcoal did not affect the results. In carrying out the experiments, we also proposed to determine whether the distribution of platinum through the depth of the grain changed in relation to the concentration of the starting solutions (i.e., definite calculated platinum content of the catalyst) and for this we prepared three series of preparations with the same charcoal grain size, but with calculated Pt contents of 20, 4, and 2%. In addition to this, experiments were also carried out to measure the catalytic activity in the dehydrogenation of cyclohexane and the hydrogenation of benzene.

EXPERIMENTAL

The catalysts were prepared on activated birchwood charcoal with a one hour activity of 25.3% with respect to ether and an ash content of 2.29%. In connection with the problems at hand, the preliminary mechanical treatment of the charcoal consisted of cutting the pieces into cubes of definite sizes, namely, with edges of 10, 6, 4, 3, and 2 mm. Separate series of catalysts were prepared from cubes of each size and the whole series thus consisted of preparations of all sizes, which were tested for catalytic activity separately. The catalysts were prepared by impregnating the charcoal with a solution of chloroplatinic acid of an appropriate concentration for the given series at room temperature. In all cases, 3 ml of solution was taken for 1 g of charcoal. After this, the catalysts were left for a day and then dried to constant weight at 120–125°. The catalysts were reduced in a stream of electrolytic hydrogen at 330° until the evolution of hydrogen chloride ceased.

The distribution of platinum through the depth of the catalyst grain was determined by the absorption of x-rays. For this purpose, sections approximately one millimeter thick were prepared from a cube of each sample; the thickness was measured accurately with a micrometer. To eliminate errors in absorption measurement, the edges of these sections were cut off in accordance with the position of the section in the cube and thus samples were obtained in which the concentration of platinum corresponded to the actual depth of occurrence of the

section in the catalyst grain. The sections were cemented to a 0.15 mm nitrocellulose film with a nitrocellulose varnish. As has already been stated, the samples were examined on a URS-50-I apparatus. Due to the fact that the concentration of platinum in the samples poorest in it was only 2%, it was necessary to develop a definite examination procedure on the basis of preliminary experiments so as to obtain comparative data in all series. It was found necessary to separate out a very fine beam from the primary beam of x-rays; for this purpose, in addition to the fine slit diaphragm on the apparatus itself, an additional lead diaphragm with a 0.5 mm cylindrical opening had to be set in front of the sample: the beam obtained passed through the center of the sample, which was set on the tip of a GUR-3 x-ray goniometer, perpendicular to the incident beam.

The absorption of x-rays was determined by an ionization method. For each measurement we determined the number of pulses without the sample, with the sample cemented to the film and with the film without sample. The exposure was controlled by a time relay and was always 128 sec at 20 kv and 3 ma with unfiltered Cu K radiation. From the data obtained we calculated the corresponding numbers of pulses per second with the intensity of the primary beam adjusted to 1000 pulses per second. Thus, for example, section No. 1 of a sample with 20% Pt and a cube edge of 10 mm gave 174 pulses per second when the primary beam in this experiment had an intensity of 975 pulses per second. When adjusted to a primary beam intensity of 1000 pulses/sec, the number of pulses for the sample was $174 \cdot 1000/975 = 178$ pulses/sec.

Experiments showed that the absorption caused by the film backing of the samples was the same and equaled 13.6% of the primary radiation. Certain, but very small errors could have arisen due to nonuniformity of thickness in the thin layer of nitrocellulose varnish and also due to the sections being not completely plane parallel. The number of pulses per second was adjusted to a section thickness of 1 mm; the calculation was carried out according to the formula

$$I = I_0 e^{-\mu D}, \qquad (I)$$

where I_0 is the primary radiation (allowing for absorption in the film, it was taken as 866 pulses/sec), I is the number of pulses/sec with the sample, μ the coefficient of attenuation by the sample, and D the sample thickness measured with a micrometer.

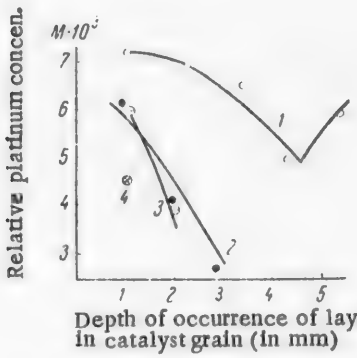

Fig. 1. Change in platinum content through the grain depth of a 20% Pt – charcoal catalyst. Measurements of catalysts grain (in mm): 1) 10, 2) 5, 3) 4, 4) 3, 5) 2.

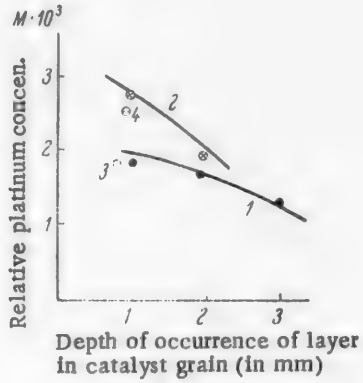

Fig. 2. Change in platinum content through the grain depth of a 4% Pt – charcoal catalyst. Notation of curves as in Fig. 1.

The attenuation coefficient of the sample was determined from this formula and the number of pulses/sec at a sample thickness of 1 mm, X, was determined from the formula $X = 866 e^{-\mu}$.

To calculate the concentration of platinum on the charcoal in the sections, Formula (I) was transposed into the formula

$$X = I_0 e^{-\frac{\mu}{\rho} M}, \qquad (II)$$

where X is the number of pulses/sec at a sample thickness of 1 mm, μ/ρ is the mass attenuation coefficient of platinum, and M corresponds to the amount of platinum in grams contained in a 1 cm^2 lamina, 1 mm thick, perpendicular to the primary beam.

Since, with the same diaphragm, which was used in all experiments, the area irradiated by x-rays was the same, the value of M changed proportionally to the concentration of platinum in different samples.

Substituting M in the expression given above for X, we obtain the final formula for the platinum concentration

$$M = \frac{\lg \frac{I_0}{x}}{\frac{\mu}{\rho} \lg e}, \qquad \text{(III)}$$

according to which its value for each sample was calculated.

The mass attenuation coefficient μ/ρ was composed of the mass scattering coefficient, which had a value of less than unity for platinum, and the absorption coefficient, which equals 205 for platinum with CuK_α radiation. Since the bulk of the primary beam, which was constant in composition, consisted of α-radiation as regards intensity, we did not introduce a correction for the absorption coefficient of β-radiation, though it was somewhat less than 205 and this led to a certain error in the absolute values, which was constant for all experiments. The absorption of a one millimeter layer of charcoal was also constant in all experiments and, as calculation showed, did not affect the course of the curves in Figs. 1-3.

DISCUSSION OF RESULTS

The results obtained are presented graphically in Figs. 1-3 for calculated platinum concentrations equal to 20, 4, and 2%, respectively; the values of $M \cdot 10^3$ are plotted along the ordinate. As the figures show, the platinum concentration falls with an increase in depth into the catalyst grain and the general picture of a fall in platinum concentration with depth into the charcoal grain is the same as obtained previously in paper [1], whose conclusions on and explanations of the phenomenon itself are confirmed by the more accurate measurements. The slope of the curves in Figs. 1-3 show that in general, the platinum concentration gradient increases with a decrease in grain of the catalyst. This conclusion differs from that arrived at in paper [1] with less accurate measurements. The course of curve 1 in Fig. 1 shows that on passing through the middle of the catalyst grain, the platinum concentration again rises, which is quite natural due to the proximity of the layer to the side of the cube opposite to the first section.

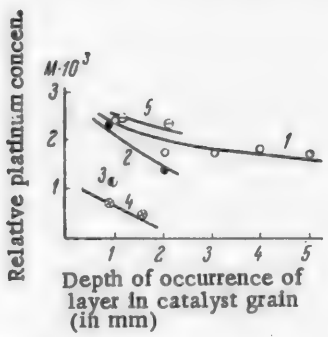

Fig. 3. Change in platinum content through the grain depth of a 2% Pt—charcoal catalyst. Notation of curves as in Fig. 1.

A comparison of the results obtained with 20% catalyst (Fig. 1) and with 4 and 2% (Figs. 2 and 3) leads to two conclusions: the distribution of platinum in the charcoal grain becomes more uniform with a decrease in the platinum concentration in the original solution for preparation of the catalysts. This is obvious from the fact that the platinum concentration gradient in the 20% catalyst is considerably greater than in the 4 and 2% samples and from the fact that with 4 and 2% Pt, extremely similar results were obtained. This result shows that the nonuniformity of platinum distribution in the charcoal grain is caused by a reduction in the concentration of the original solution in the depth of the charcoal grain as a result of adsorption of H_2PtCl_6 from it by charcoal layers lying above. The practical conclusion from the results obtained is that for the preparation of a Pt—C catalyst with the greatest concentration of platinum in the surface layers it is necessary to start from concentrated platinum solutions. Dilute solutions should be used for a more uniform distribution of platinum inside the grain.

It should be added that the picture described for the distribution of metal in an impregnated catalyst is characteristic of not only the carrier charcoal. An analogous distribution, which was even more sharply expressed and readily visible to the naked eye, occurred in Pd–Al_2O_3 catalysts and some Pt–Al_2O_3 catalysts, prepared by impregnation methods [2]. The more sharply expressed distribution in these cases is readily explained by the basicity of the carrier relative to platinum or palladium solutions.

Catalytic experiments were carried out in a normal flow apparatus. Cyclohexane was dehydrogenated in a slow stream of hydrogen at 300-305° and benzene was hydrogenated at 175-180° in a stream of hydrogen, whose excess was 40% over the theoretically required amount of H_2 for complete hydrogenation of benzene. In both cases, the extent of the conversion was followed refractometrically [3]. The experimental data are presented in the table. For a consideration of the data presented in it, it follows that with catalysts containing 20 and 4% Pt,

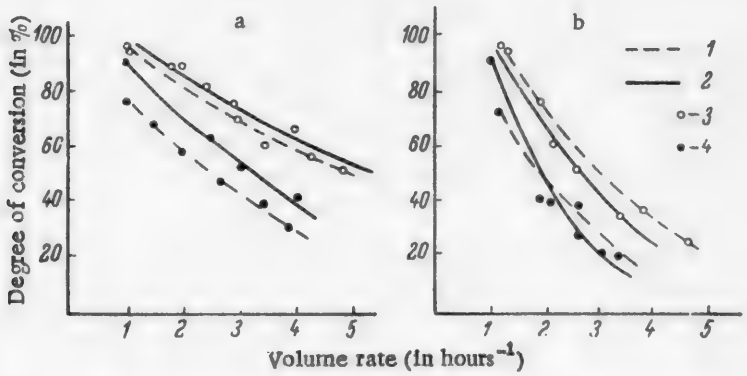

Fig. 4. Effect of volume rate on catalytic activity of Pt–charcoal with various grain sizes and platinum contents in the dehydrogenation of cyclohexane (a) and hydrogenation of benzene (b). 1) 2% Pt, 2) 20% Pt, 3) grain 3 mm, 4) grain 10 mm.

the extent of cyclohexane dehydrogenation at a volume rate of 1 hour^{-1} depends very little on the grain size, while the hydrogenation of benzene on the same catalysts differs by 10 to 15%. The catalyst with a 2% Pt content and a grain size of 10 mm was found to be less active than the first two catalysts with the same grain sizes. Catalysts with grain sizes of H and 3 mm had practically the same activity at all platinum concentrations, both in the dehydrogenation of cyclohexane and the hydrogenation of benzene. This may be due to the long contact time at a volume rate of 1 hour^{-1}, at which equilibrium concentrations are attained practically. On the

Dehydrogenation of C_6H_{12} and Hydrogenation of C_6H_6 at a Volume Rate of 1 hour^{-1} on Platinized Charcoals with Different Platinum Concentrations in Relation to Grain Size

Catalyst	Extent of conversion (in %)							
	dehydrogenation of C_6H_{12}, 300-305°				hydrogenation of C_6H_6, 180°			
	Catalyst grain size (in mm)							
	10	6	4	3	10	6	4	3
20% Pt–C	92.6	91.5	98.0	98.8	85.0	86.6	100	100
4% Pt–C	90.0	95.0	98.6	94.8	87.0	92.0	99.2	100
2% Pt–C	78.6	90.8	93.4	95.0	74.0	92.0	93.0	97.0

other hand, considering the difference in the platinum concentrations in the three series of catalysts, this effect may be ascribed to the fact that the reaction proceeds in the kinetic region where diffusion to active centers does not play any part. There are grounds for this idea, since the degree of conversion changed little with a change in the grain size (see table).

In connection with what has been said, further experiments were carried out with catalysts containing 20 and 2% Pt and with a grain size of 10 and 3 mm. Their activity was determined at higher volume rates. The course of the changes in the degree of conversion in both reactions with an increase in volume rate of hydrocarbon throughput is presented in Fig. 4. As can be seen, the degree of conversion falls rapidly with an increase in volume rate, whereby the changes for 10 and 3 mm grains are quite similar, though the fall of the curves for 10 mm grains is somewhat steeper. Thus, with an increase in the volume rate, certain differences appear in the activity of 10 and 3 mm grains, which increase with a decrease in the contact time. Since the dehydrogenation of cyclohexane is a zero order reaction, the results obtained show that the reaction does not proceed in a purely kinetic region and that diffusion factors are superposed.

SUMMARY

From the absorption of x-rays, measured by an ionization method on a URS-50-I apparatus, we determined the distribution of platinum through the depth of the charcoal grain in impregnated Pt–C catalysts with 20, 4, and 2% Pt and charcoal grain sizes of 2-10 mm. A fall in platinum concentration from the surface into the depth of the grain was confirmed and it was established that the platinum concentration gradient through the grain depth decreased with a decrease in the platinum concentration of the original solution: dilute solutions gave catalysts with more uniform metal distribution.

It was shown that at low volume rates, the concentration and distribution of platinum did not affect the activity in the hydrogenation of benzene and the dehydrogenation of cyclohexane, but they affected the degree of conversion at higher volume rates.

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SYNTHESIS OF 1-HYDROXYALKYL-2,5-DIMETHYLPIPERIDINES

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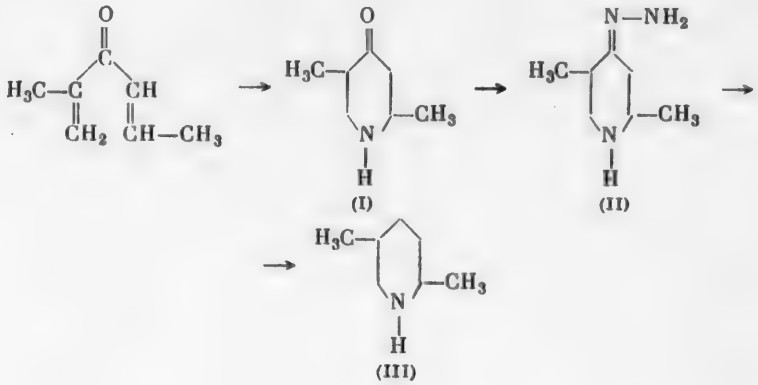
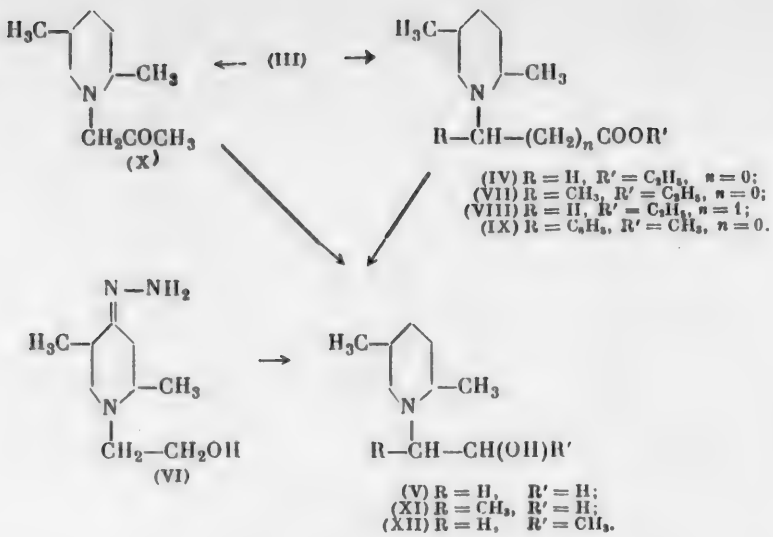
2,5-Dimethyl-4-piperidone (I), obtained by I. N. Nazarov's method from propenyl isopropenyl ketone and ammonia [1, 2], has been used for the preparation of amino alcohols, which may be used as intermediates in syntheses of analgesics (Phenadone type), local anesthetics (Surfocaine and Methicaine type) and spasmolytics (Artane type), containing a ring-substituted piperidyl radical as the amine residue.



2,5-Dimethylpiperidine (III) was obtained in 75% yield by a Kizhner reduction of the hydrazone (II) of 2,5-dimethyl-4-piperidone. The introducion of a hydroxyalkyl substituent at the nitrogen of the piperidine ring was achieved by several methods. 1-β-Hydroxyethyl-2,5-dimethylpiperidine (V) was obtained both by the direct interaction of piperidine (III) with ethylene chlorohydrin and by lithium aluminum hydride reduction of the ethyl ester of 2,5-dimethylpiperidyl-1-acetic acid (IV), which was obtained from piperidine (III) and ethyl bromoacetate. Kizhner reduction of the hydrazone (VI) of 1-β-hydroxyethyl-2,5-dimethyl-4-piperidone also led to the formation of amino alcohol (V), but in this case the yield did not exceed 35%. The ethyl esters of α- (VII) and β- (VIII) 2,5-dimethylpiperidyl-1-propionic acids were obtained by condensing esters of the appropriate bromine-substituted propionic acids with piperidine (III). An analogous method was used for synthesizing the methyl ester of 2,5-dimethylpiperidyl-1-phenylacetic acid (IX) and 1-acetonyl-2,5-dimethylpiperidine (X).

The ethyl ester of α-2,5-dimethylpiperidyl-1-propionic acid and also 1-acetonyl-2,5-dimethylpiperidine were reduced with lithium aluminum hydride; amino ketone (X) was also reduced with sodium in alcohol to the following amino alcohols: 1-α-methyl-β-hydroxyethyl-2,5-dimethylpiperidine (XI) and 1-β-hydroxypropyl-2,5-dimethylpiperidine (XII). Condensation of 2,5-dimethylpiperidine with propylene oxide at 60-70° in an alcohol dioxane solution led to the formation of a mixture of amino alcohols (XI) and (XII). It is interesting to note that 2,5-dimethyl-4-piperidone did not react with propylene oxide under the same conditions.



EXPERIMENTAL

2,5-Dimethyl-4-piperidone (I) was obtained by the procedure described previously [2].

2,5-Dimethylpiperidine (III). A mixture of 70 g of 2,5-dimethyl-4-piperidone (I) and 83 ml of hydrazine hydrate was heated on a boiling water bath for 30 minutes. After removal of the excess hydrazine hydrate, the reaction product was vacuum distilled. We obtained 38.8 g of hydrazone (II) as a clear viscous liquid with b.p. 110-125° (2 mm). The hydrazone of 2,5-dimethyl-4-piperidone was used for subsequent work without additional purification. 38.8 g of hydrazone (II) and 28.2 g of powdered potassium hydroxide were heated to 200°. Heating was accompanied by vigorous evolution of nitrogen and distillation of the reaction product at 105-143°. A second distillation yielded 24 g of 2,5-dimethylpiperidine (III) with b.p. 137-138°.

The hydrochloride had m.p. 193-195° (from acetone).

Found %: N 9.70, 9.81; Cl 23.74, 23.67. $C_7H_{16}NCl$. Calculated %: N 9.36; Cl 23.74.

In preparing the hydrazone of 2,5-dimethyl-4-piperidone, we also isolated the azine of 2,5-dimethyl-4-piperidone with b.p. 145-150° (3 mm).

Found %: N 22.16, 22.39. $C_{14}H_{26}N_4$. Calculated %: N 22.40.

Ethyl ester of 2,5-dimethylpiperidyl-1-acetic acid (IV). A mixture of 27.4 g of 2,5-dimethylpiperidine (III), 49.6 g of potassium carbonate, 40.3 g of bromoacetic acid and 50 ml of acetone was heated for 8.5 hours on a boiling water bath. The reaction product was extracted with ether. Distillation yielded 37.7 g of ester (IV) with b.p. 78-80° (2 mm) $n^{20}D$ 1.4531.

Found %: N 6.62, 6.75. $C_{11}H_{21}O_2N$. Calculated %: N 7.03.

1-β-Hydroxyethyl-2,5-dimethylpiperidine (V). a) Over a period of 2 hours, 23.4 g of the ethyl ester of 2,5-dimethylpiperidyl-1-acetic acid (IV) in 100 ml of absolute ether was added dropwise to 52.5 g of a solution of lithium aluminum hydride in ether, cooled to −70°. The temperature of the reaction mixture rose to −30° and after 1 hour's stirring, the reaction products were decomposed successively with 30 ml of ethyl acetate and 50 ml of a saturated solution of ammonium chloride. The ether layer was separated and dried. Removal of the ether and vacuum distillation yielded 13.35 g of amino alcohol (V) with b.p. 73-74° (2 mm), $n^{20}D$ 1.4694.

The picrate had m.p. 93-94° (from alcohol).

Found %: N 14.60, 14.55. $C_{15}H_{22}O_8N_4$. Calculated %: N 14.50.

b) A mixture of 12.7 g of 2,5-dimethylpiperidine (III), 22 g of potassium carbonate, 10 g of ethylene chlorohydrin and 20 ml of acetone was heated on a boiling water bath for 12.5 hours. The reaction products were extracted with ether and vacuum distilled. We obtained 7.8 g of (V) with b.p. 73-75° (2 mm).

c) 6.2 g of the hydrazone (VI) of 1-β-hydroxyethyl-2,5-dimethyl-4-piperidone (b.p. 165-170° at 3 mm) and 3 g of potassium hydroxide were heated to 200°. Heating was accompanied by vigorous evolution of nitrogen and distillation of the reaction product. We obtained 1.9 g of (V) with b.p. 72-74° (2 mm).

Ethyl ester of α-2,5-dimethylpiperidyl-1-propionic acid (VII). With stirring and cooling, 62.5 g of ethyl α-bromopropionate was added to a mixture of 30 g of 2,5-dimethylpiperidine (III), 30.2 g of potassium carbonate and 20 ml of dry acetone. The mixture was heated for 13.5 hours at the boiling point of acetone and the reaction products extracted with ether and then vacuum distilled. We obtained 50 g of ester (VII).

B.p. 84-86° (2 mm), $n^{20}D$ 1.4540, d^{20}_4 0.9551, MR 60.53; calc. 60.44. Found %: N 6.56, 6.50. $C_{12}H_{23}O_2N$. Calculated %: N 6.57.

The picrate had m. p. 113-140° (from alcohol).

Found %: N 12.94, 12.90. $C_{18}H_{26}O_9N_4$. Calculated %: N 12.67.

Ethyl ester of β-2,5-dimethylpiperidyl-1-propionic acid (VIII). 19.2 g of 2,5-dimethylpiperidine (III), 36 g of potassium carbonate, 65 ml of acetone and 40 g of ethyl β-bromopropionate were boiled for 12 hours. The reaction products were extracted with ether and then vacuum distilled. We obtain 28.8 g of ester (VIII) with b.p. 116-118° (3 mm).

Found %: N 6.20, 6.25. $C_{12}H_{23}O_2N$. Calculated %: N 6.57.

Methyl ester of 2,5-dimethylpiperidyl-1-phenylacetic acid (IX). A mixture of 6.1 g of 2,5-dimethylpiperidine (III), 13.3 g of methyl bromophenylacetate, 12.5 g of potassium carbonate and 20 ml of acetone was heated for 15 hours at the boiling point of acetone. Distillation of the reaction products which were extracted with ether yielded 5.3 g of ester (IX) with b.p. 142-148° (4 mm).

Found %: N 5.50, 5.28. $C_{16}H_{23}O_2N$. Calculated %: N 5.38.

1-Acetonyl-2,5-dimethylpiperidine (X). With cooling in ice water and stirring, 19.7 ml of monobromoacetone was added dropwise to a mixture of 18.2 g of 2,5-dimethylpiperidine, 33.4 g of potassium carbonate and 30 ml of acetone. After being stirred for 2 hours at room temperature, the reaction products were extracted with ether and then vacuum distilled. We obtained 20 g of 1-acetonyl-2,5-dimethylpiperidine (X) with b.p. 67-68° (3 mm), $n^{20}D$ 1.4558.

The picrate had m.p. 101-104° (from alcohol).

Found %: N 14.12, 13.84. $C_{16}H_{22}O_8N_4$. Calculated %: N 14.07.

1-α-Methyl-β-hydroxyethyl-2,5-dimethylpiperidine (XI). Over a period of 1.5 hours, a solution of 30 g of the ethyl ester of α-2,5-dimethylpiperidyl-1-propionic acid in 200 ml of ether was added to 125 g of a solution of lithium aluminum hydride in ether, cooled to −70°. The temperature of the mixture rose to −30° and after being stirred for 1 hour, the reaction products were successively decomposed with 30 ml of ethyl acetate and 60 ml of a saturated solution of ammonium chloride. The ether layer was separated and dried. Vacuum distillation of the reaction products yielded 19.9 g of (XI).

B.p. 85-87° (2.5 mm), $n^{20}D$ 1.4721, d^{20}_4 0.9396, MR 51.13; calc. 51.64. Found %: N 8.57, 8.36. $C_{10}H_{21}ON$. Calculated %: N 8.18.

1-β-Hydroxypropyl-2,5-dimethylpiperidine (XII). a) Over a period of 1 hour, 15 g of 1-acetonyl-2,5-dimethylpiperidine (X) in 100 ml of ether was added to 125 g of a solution of lithium aluminum hydride in ether, cooled to −70°. The temperature of the mixture rose to −30° and after being stirred for 1 hour, the reaction products were decomposed successively with 20 ml of ethyl acetate and 40 ml of a saturated solution of ammonium chloride. The ether layer was separated and dried. Vacuum distillation of the reaction products yielded 11.1 g of (XII) with b.p. 79-81° (3 mm), $n^{20}D$ 1.4594.

Found %: N 8.25, 7.90. $C_{10}H_{21}ON$. Calculated %: N 8.19.

b) 9 g of sodium was very rapidly added to a vigorously boiling solution of 22 g of (X) in 100 ml of anhydrous alcohol. After the solution of all the sodium, the reaction was made acid to Congo with 15% hydrochloric acid with cooling. The alcohol was removed in vacuum, the neutral reaction products extracted with

ether and the aqueous layer treated with alkali and extracted with ether. Distillation of the reaction products yielded 13 g of (XII) with b.p. 79-81° (3 mm).

Interaction of propylene oxide with 2,5-dimethylpiperidine. Over a period of 15 minutes, 4.5 g of propylene oxide was added at 60-70° to a mixture of 8.7 g of 2,5-dimethylpiperidine, 15 ml of dioxane, 1.5 ml of alcohol, and 1 ml of water. Stirring was continued at the same temperature for 0.5 hour. Distillation of the reaction products yielded 1.2 g of the original 2,5-dimethylpiperidine and 3.3 g of condensation product [a mixture of 1-α-methyl-β-hydroxyethyl-2,5-dimethylpiperidine (XI) and 1-β-hydroxypropyl-2,5-dimethylpiperidine (XII)] with b.p. 69-74° (2.5 mm).

Found %: N 8.27, 8.47. $C_{10}H_{21}ON$. Calculated %: N 8.19.

The picrate had m.p. 101-111° (from alcohol).

Found %: N 13.87, 14.28. $C_{16}H_{24}O_8N_4$. Calculated %: N 14.00.

SUMMARY

2,5-Dimethyl-4-piperidone was used for synthesizing new amino alcohols, 1-hydroxyalkyl-2,5-dimethylpiperidines, which are intermediates in the synthesis of physiologically active substances.

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COMPLEXES OF VINYLACETYLENE WITH CUPROUS CHLORIDE IN HYDROCHLORIC ACID SOLUTIONS

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Chloroprene may be synthesized from vinylacetylene by interaction of the latter with a hydrochloric acid solution of cuprous chloride [1, 2]. The latter apparently forms reactive complexes with vinylacetylene. Such complexes are readily produced both in neutral and acid solutions by the interaction of CuCl with a series of unsaturated compounds [3-7]. As is known, the solubility of CuCl in hydrochloric acid or aqueous solutions of metal chlorides is explained by the formation of complexes of various compositions [8-10].

The investigation was aimed at studying the preparation conditions and also the composition of complexes formed by vinylacetylene with cuprous chloride in hydrochloric acid solutions. It was established that crystalline complexes of vinylacetylene with cuprous chloride of various compositions were formed in these solutions. Due to the formation of these compounds, an increase in the solubility of cuprous chloride in hydrochloric acid by its interaction with vinylacetylene was observed.

The composition of the complexes depended on the concentration of hydrochloric acid in the solution and did not depend on temperature. The crystalline compounds obtained by the interaction of vinylacetylene with cuprous chloride in 10% hydrochloric acid had the average composition 65.4% CuCl and 34.5% C_4H_4, which corresponds to the formula $CuCl \cdot C_4H_4$. The compounds obtained with solutions of CuCl in 20% hydrochloric acid had a lower vinylacetylene content. Their average composition was 79.2% CuCl and 20.8% C_4H_4 and correspond to the formula $(CuCl)_2 \cdot C_4H_4$. As regards the complex obtained with a solution in 15% HCl, according to its composition it was apparently a mixture of the two complexes mentioned above. Simultaneously, it was established that a considerable part of the vinylacetylene remained in solution in a complex-bound state and could be isolated from the latter by desorption. When this solution was saturated with hydrogen chloride, decomposition of the complex occurred with the evolution of vinylacetylene, and chloroprene was partly formed.

On the basis of these data, it was supposed that in a hydrochloric acid solution of CuCl, interaction of it with vinylacetylene formed a complex compound containing both hydrogen chloride and vinylacetylene, which could displace each other from the complex.

To demonstrate the possible existence of a more complicated complex, we studied the interaction of hydrogen chloride with the crystalline compounds with the compositions $CuCl \cdot C_4H_4$ and $(CuCl)_2 \cdot C_4H_4$.

EXPERIMENTAL

Hydrochloric acid solutions of cuprous chloride were prepared by dissolving dry cuprous chloride in chemically pure hydrochloric acid of various concentrations (10, 15 and 20%). To prevent oxidation, we stored the solutions over copper turnings in an atmosphere of carbon dioxide.

The vinylacetylene used was first freed from acetaldehyde by treatment with a 2% solution of hydroxylamine. The washed and dried vinylacetylene was redistilled twice.

For studying the effect of vinylacetylene on the solubility of CuCl, a sample of dry CuCl was loaded into a flask with two outlets. The flask was then evacuated and weighed and into it was sucked a previously prepared saturated solution of CuCl in hydrochloric acid. The flask was then connected through a distributor to a burette with gaseous vinylacetylene and placed in a thermostat at 20°. Vinylacetylene was gradually introduced through

a tap. Gradual solution of the CuCl precipitate was then observed. The data obtained are presented in Table 1.

From the data presented it follows that with low concentrations of HCl in the solution (6-9%), the solubility of CuCl was increased by 60-80%. At high concentrations of HCl (12-20%), the solubility of CuCl increased by 30-35%.

Preparation of Binary Complexes

The complexes were usually prepared in an apparatus described by L. G. Tsyurikh and A. A. Ginzburg [11]. To tap a of the distributor was connected a flask (see figure) with two ground-glass taps. The distributor and flask were evacuated and the flask weighed. Through tap c in the flask was sucked a previously prepared solution of cuprous chloride in hydrochloric acid of a given concentration and the flask again weighed. The sample of solution

TABLE 1

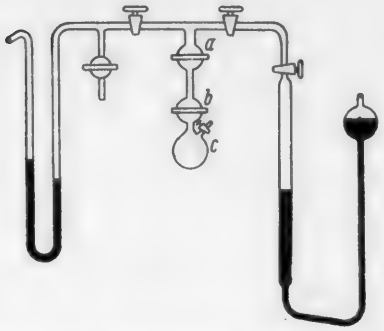
Effect of Vinylacetylene on the Solubility of CuCl at 20° (average data)

Composition of original saturated solution (in %)		Vinyl-acetylene passed (in ml)	Composition of solution (in %) after absorption of vinylacetylene	
CuCl	HCl		CuCl	HCl
1.89	6.28	208	3.51	5.81
3.27	8.55	300	4.46	7.69
4.92	9.79	269	8.38	7.63
5.49	10.25	195	8.93	8.51
6.85	12.47	270	10.71	10.64
9.92	14.79	374	14.71	13.20
12.24	15.06	270	15.07	14.29
15.57	17.92	380	19.25	15.81
18.89	20.10	450	24.11	17.10

taken was adjusted to the required temperature and then vinylacetylene passed into the flask through tap b from the gas burette. When the first portions of vinylacetylene, which were adsorbed very rapidly, were passed in, a precipitate of CuCl formed on cooling, but this gradually disappeared and the solution acquired a yellow color. With further introduction of vinylacetylene, its absorption slowed and a white, crystalline precipitate began to form, which did not dissolve when the temperature was raised to 20-25°. Vinylacetylene was introduced until absorption ceased, as indicated by the manometer. A constant temperature was maintained during the whole experiment. The amount of vinylacetylene absorbed was determined from the weight of the flask. The crystalline precipitate was filtered from the mother solution at 20-25° without the admission of air in order to prevent oxidation. The amount of crystalline complex usually did not correspond to the amount of vinylacetylene absorbed since a considerable portion of the vinylacetylene was present in the mother solution in the form of a complex with cuprous chloride. The latter was confirmed by determining the amount of bound vinylacetylene by its desorption from the mother solution. Desorption was carried out by flushing with carbon dioxide or nitrogen, at first in the cold and then with heating up to 90°. The amount of vinylacetylene liberated was determined by difference in weight before and after desorption and also by condensation at liquid air temperatures. Where CO_2 was used, the mixture of gases was passed through alkali and then the vinylacetylene collected in a burette over mercury.

The vinylacetylene was determined by absorption in an alkaline solution of $Hg(CN)_2$. After desorption of the vinylacetylene, the mother solution was analyzed for Cu (iodometrically) and HCl (alkalimetrically). The crystalline precipitate, which was first cooled and separated from the mother solution, was washed with anhydrous alcohol and ether in the first experiments. The alcohol and ether were flushed with CO_2 to remove air. The washed crystals were dried at room temperature in a stream of CO_2. The emergent gas was passed through Ilosvay's

solution and in this way the whole of the vinylacetylene remaining in the crystals after washing was trapped. After separation of the vinylacetylene from them, the crystalline precipitates were analyzed for Cu and Cl (by Volhard's method).



Scheme of apparatus for preparing complexes. Explanation in text.

TABLE 2

Composition of Complexes Obtained by Interaction of Vinylacetylene with a Solution of CuCl in HCl (composition 4.54% CuCl and 10.08% HCl)

Temperature	Composition of crystals after drying (in %)	
	CuCl	C_4H_4
+5°	66.6	33.4
+5	67.69	32.31
0	65.26	34.72
0	65.13	34.81
−5	66.19	33.79
−5	64.96	30.01
Average data	65.97	34.03

The wash alcohol and ether were assayed for vinylacetylene (by Ilosvay's method), copper, HCl, and Cl. The complexes obtained by passing vinylacetylene through a saturated solution of cuprous chloride in 10% hydrochloric acid were investigated by the given procedure. The CuCl content of the starting solution was 5%. Data of these experiments are given in Table 2.

It should be noted that when the crystals were washed with alcohol and ether, part of the vinylacetylene and also a very small amount of cuprous chloride extracted. Therefore, in calculating the composition of the complexes, appropriate corrections were introduced.

In subsequent experiments, the crystalline precipitates were investigated in the following way: the crystalline complex obtained was washed with anhydrous alcohol and ether, saturated with vinylacetylene at the temperature of the experiment. The vinylacetylene content of the alcohol and ether was determined before washing and the Cu, Cl, HCl,and vinylacetylene were determined after washing. As the results of analyzing the alcohol and ether show, their vinylacetylene contents did not change during washing at −5°-(+5°). Having been washed with alcohol and ether, the crystals were dried at room temperature in a stream of vinylacetylene. For this purpose, a flask with the washed crystals was attached through a tap to a reflux condenser, which, in its turn, was attached to a flask with liquid vinylacetylene. The emergent vinylacetylene was trapped by condensation at −78° (solid CO_2), when the amount of vinylacetylene passed corresponded to the amount condensed. Thus, it was established that the crystals neither absorbed nor liberated vinylacetylene during drying. The color of the crystals did not change during drying. The dried complexes were decomposed with dilute HNO_3 and HCl or carbon dioxide. Decomposition was carried out in the following way: the flask with the dried crystals was connected to 2-3 mercury gas burettes. To the other tap of the flask was attached a funnel, through which 15% nitric acid was introduced in small portions. Evolution of gas and solution of the precipitate began immediately. The gas was collected in the burette. Decomposition was carried out in the cold and then the flask was heated on a water bath at 70° until the evolution of gas ceased. The gas was flushed from the flask into the burette by filling with water or acid of the same concentration. The vinylacetylene content of the gas was determined by absorption with an alkaline solution of $Hg(CN)_2$. The amount of vinylacetylene obtained was close to theoretical. Decomposition of the dry crystals with hydrochloric acid gave a smaller amount of vinylacetylene. The latter is apparently explained by the fact that during decomposition of the complexes, the vinylacetylene partially reacted with hydrochloric acid to form chloro derivatives.

The complexes were also decomposed in a stream of carbon dioxide as indicated above. The remains of the crystals after decomposition with acids were analyzed for copper and chlorine content. We investigated the

crystalline complexes obtained by interaction of vinylacetylene with solutions of cuprous chloride in 10, 15, and 20% hydrochloric acid at temperatures of −5, 0, and +5°. The data obtained are presented in Table 3.

TABLE 3

Analysis of Complexes Obtained by Interaction of Vinylacetylene with a Saturated Solution of CuCl in Hydrochloric Acid

Temperature	Concen. of HCl (in %)	Composition of original solution (in %)		Composition of crystals after drying (in %)		Comments
		CuCl	HCl	CuCl	C_4H_4	
0°	10	5.68	10.01	66.5	33.56	
+5		5.50	10.05	66.8	33.22	Decomp. HNO_3
−5		5.51	10.50	64.17	34.85	
		Average		65.82	33.88	
0	15	10.34	14.57	74.51	25.50	
−5		10.39	14.65	73.63	26.26	Decomp. HNO_3
+5		9.70	14.50	75.73	24.31	
		Average		74.62	25.02	
0	20	16.31	19.78	79.10	20.90	Decomp. CO_2
+5		15.25	19.55	80.30	19.71	
−5		16.36	19.78	79.24	20.72	
		Average		79.54	20.44	

Elementary Analysis of Complexes Obtained with Hydrochloric Acid

With 10% HCl

Found %: C 31.47; H 2.68; Cl 23.34; Cu 42.74. $CuCl \cdot C_4H_4$. Calculated %: C 31.78; H 2.63; Cl 23.51; Cu 42.08.

With 20% HCl

Found %: C 19.03; H 1.62; Cl 27.92; Cu 51.80. $(CuCl)_2 \cdot C_4H_4$. Calculated %: C 19.20; H 1.60; Cl 28.40; Cu 50.80.

Preparation of Ternary Complexes

Dry hydrogen chloride from a burette was passed through a flask with dry complex. The emergent gas was collected in a receiver over mercury and analyzed for HCl and C_4H_4 content. The crystalline compounds obtained were examined for vinylacetylene, hydrogen chloride, and cuprous chloride content. For this purpose, the products obtained were decomposed by heating for 1-2 hours on a boiling water bath in the same flask in which they were synthesized. The gas liberated was collected over mercury and analyzed for HCl and C_4H_4 content. The crystals changed color during decomposition. They changed from a yellowish color to a greyish white. The precipitate contained no hydrogen chloride after decomposition in all cases.

As a result, the following analytical data were obtained for the product of hydrogen chloride interaction with the complex $(CuCl)_2 \cdot C_4H_4$.

Found %: CuCl 81.53; 81.03; C_4H_4 10.87, 11.06; HCl 7.31, 7.06. $(CuCl)_4 \cdot C_4H_4 \cdot HCl$. Calculated %: CuCl 81.66; C_4H_4 10.77; HCl 7.56.

These data show that the action of hydrogen chloride caused replacement of approximately 50 mol. % of the vinylacetylene in the complex by hydrogen chloride. Slight deviation of the composition of the complex obtained from that proposed is explained by its instability. This instability is shown much more strongly by complexes obtained by interaction of hydrogen chloride with the binary complex with the composition $CuCl \cdot C_4H_4$.

Analysis of the product of hydrogen chloride interaction with the complex $CuCl \cdot C_4H_4$ gave the following data.

Found %: CuCl 80.75, 80.90; C_4H_4 9.83, 10.09; HCl 7.03, 6.15.

As the data presented shows, this compound contained slightly less vinylacetylene and hydrogen chloride, but it can be assumed that in this case also, a compound was obtained with the same composition as in the case of hydrogen chloride interaction with the complex $(CuCl)_2 \cdot C_4H_4$.

The deficiency of vinylacetylene and hydrogen chloride is apparently explained by the instability of the original complex $CuCl \cdot C_4H_4$. The latter is confirmed by the fact that by decomposition of the complex $CuCl \cdot C_4H_4$ immediately after its preparation, we were able to isolate 34.5% of vinylacetylene, which corresponds to the composition $CuCl \cdot C_4H_4$. When the complex stood for some time, the amount of vinylacetylene liberated fell and after 4-6 hours standing, the complex yielded not more than 25% of vinylacetylene, which is apparently caused by polymerization of the latter.

SUMMARY

1. The interaction of vinylacetylene with saturated solutions of cuprous chloride in hydrochloric acid of various concentrations at temperatures of −5, 0 and +5° yielded crystalline complexes with the compositions $CuCl \cdot C_4H_4$ and $(CuCl)_2 \cdot C_4H_4$.

2. The composition of the complex depended on the acidity of the solution and not on the temperature.

3. It was established that in the action of hydrogen chloride on complexes with the compositions $(CuCl)_2 \cdot C_4H_4$ and $CuCl \cdot C_4H_4$, part of the vinylacetylene was replaced by hydrogen chloride to form a crystalline ternary complex with the composition $(CuCl)_4 \cdot C_4H_4 \cdot HCl$.

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INVESTIGATIONS IN THE FIELD OF CONJUGATED SYSTEMS

CV. TELOMERIZATION OF BUTADIENE WITH CHLOROPRENE HYDROCHLORIDE (1,3-DICHLOROBUTENE-2)

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The search for ways of using 1,3]dichlorobutene-2, which is formed as a side product in the production of chloroprene, has been the subject of much work [1], in particular, a series of recently published investigations by A. L. Klebanskii, A. G. Sayadyan, and M. G. Barkhudaryan on the telomerization of this hydrochloride with butadiene, isoprene, and chloroprene [2]. In one of these articles it was stated that the telomerization of 1,3--dichlorobutene-2 with butadiene yielded predominantly the 1,4-adduct. This conclusion does not agree with our observation of the order of addition of unsaturated halogen derivatives (crotyl chloride, 2-chloropentene-3 and prenyl chloride) to butadiene: in all cases we found the formation of 1,2- and 1,4-addition products [3-5].

In order to elucidate this problem, we telomerized, 1,3-dichlorobutene-2 with butadiene under our usual conditions in the presence of stannic chloride [3-6]; the data obtained thus differed sharply from those reported by the above authors [2].

The telomerization products with the composition $C_8H_{12}Cl_2$ boiled at 20-25° higher (10 mm) than reported by A. L. Klebanskii and his co-workers. Distillation of them yielded approximately equal amounts of two fractions, of which the first was predominantly the 1,2-adduct (3,7-dichlorooctadiene-1,6) and the second predominantly the 1,4-adduct (1,7- dichlorooctadiene-2,6).

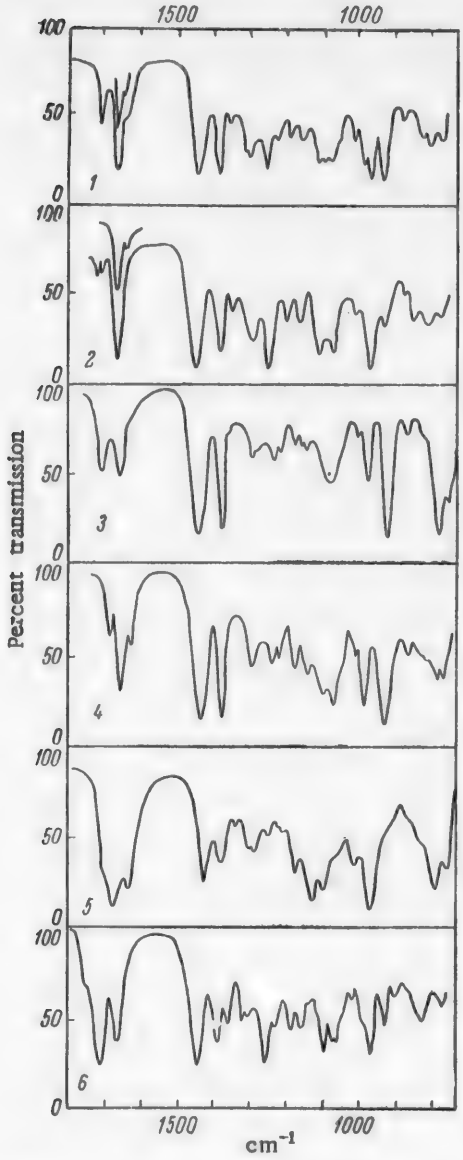
The first fraction underwent a Sommelet reaction to the extent of 28-29% after 100 hours and its infrared spectrum showed well expressed frequencies of a vinyl group (6100 – overtone, 1638, 986 and 927 cm^{-1}). Judging by the spectrum, the substance contained a small amount of a carbonyl compound with an unconjugated carbonyl group (frequency 1720 cm^{-1}).

The second fraction underwent a Sommelet reaction to the extent of 78% over the same time. Its infrared spectrum did not show the frequency of 986 cm^{-1}; the frequency of 6100 cm^{-1} was of very low intensity; on the other hand, the intensity of the grouping $-CH=CH-$ (966 cm^{-1}) increased sharply. The carbonyl compound content of this fraction was minute.

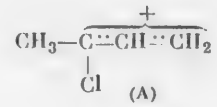
Judging by the spectrum and the melting point of the 2,4-dinitrophenylhydrazone, the Sommelet reaction gave the same aldehyde, 7-chlorooctadien-2,6-al, with the two fractions. In the infrared spectrum of this aldehyde, the carbonyl group produced the very intense frequency of 1685 cm^{-1} and the grouping $-CH=CH-$, the frequencies of 973 and 1635 cm^{-1}.

According to the spectrum, the residue from the Sommelet reaction with both fractions was the 1,2-product, practically free from the 1,4-adduct (the frequency of 966 cm^{-1} disappeared completely), but containing impurities, in particular, of carbonyl compounds.

Hydrogenation of the whole adduct $C_8H_{12}Cl_2$ over $Pd/CaCO_3$ yielded n-octane, which was identified with an authentic sample by constants and infrared spectrum. The absorption spectrum of our sample differed from the authentic one only in a slightly greater intensity of the frequency at 1132 cm^{-1}. The characteristic frequencies of 3-methylheptane, which could have been formed as a result of hydrogenation of the addition product of the allyl isomer of 1,3-dichlorobutene-2 (3,3-dichlorobutene-1) to butadiene, were not detected. Consequently, the chlorine atom in position 3 makes this position in the conjugated ion (A) inactive.



Infrared transmission spectra. 1) Fraction 89-91° (10 mm); 2) fraction 98-102° (10 mm); 3) residue after Sommelet reaction on fraction 89-91° (10 mm); 4) residue after Sommelet reaction on fraction 98-102° (10 mm); 5) 7-chlorooctadien-2,6-al; 6) fraction 75-95° (10 mm) of telomer obtained according to data in [2].



(A)

Thus, this investigation showed that contrary to the data in [2], 1,3-dichlorobutene-2 added to butadiene in the same order as crotyl chloride, i.e., in the 1,2- and 1,4-positions. There were no essential differences between the adducts $C_8H_{12}Cl_2$ and the higher telomers.

In an experiment carried out in strict accordance with the instructions of A. L. Klebanskii and his co-workers, the same product was obtained, but in considerably lower yield and with traces of a carbonyl compound, apparently the ketone produced as a result of hydrolytic cleavage of the chlorine atom at the double bond during treatment of the reaction product with water in the presence of ferric chloride (frequency 1711 cm^{-1}).

EXPERIMENTAL

The 1,3-dichlorobutene-2 used in the present work had the constants: b.p. 127-128°, d^{20}_4 1.1494, $n^{20}D$ 1.4730, which agree with literature data [7]. Technical butadiene was used.

In one of the experiments, 7.8 g of stannic chloride in 10 ml of methylene chloride was added to 108 g of butadiene (2 mole) and 250 g of 1,3-dichlorobutene-2 (2 mole) in 200 ml of methylene chloride with the mixture at −5°. The reaction was carried out at 20-23° until the increase in specific gravity was 0.076, which required 6.5 hours in the normal apparatus [6]. The butadiene losses did not exceed 5-7 g. Telomerization was stopped with pyridine.

Distillation of the mixture of telomers obtained yielded about 30 g of product with the composition $C_8H_{12}Cl_2$ and about 88 g of higher telomers. The conventional degree of telomerization was 34%.

Further fractionation (at 10 mm) of the dichloride $C_8H_{12}Cl_2$ yielded the following fractions: 1st up to 89°, 3.8 g; 2nd 89-91°, 8.4 g; 3rd 91-98°, 3.1 g; 4th 98-102°, 10.4 g; 5th 102-110°, 2.5 g; residue 5.2 g. For distillation, we took 36.2 g of material.

For the 2nd fraction we found:

d^{20}_4 1.0560, $n^{20}D$ 1.4830, MR 48.44; calc. 47.96. Found %: C 53.66, 53.75; H 7.18, 7.18; Cl 40.88. $C_8H_{12}Cl_2$. Calculated %: C 53.65; H 6.73; Cl 39.60.

After 100 hours, this fraction underwent the Sommelet-Leets reaction [8] to the extent of 28.15 and 29.08%; 1.32 and 1.33 double bonds were found by Kaufmann's method.

IR spectrum: 772, 797, 820 av, 875 av, 927 s, 966 s, 986 s, 1012 av, 1069, 1089, 1105 s, 1147 av, 1160 w, 1184 av, 1218 av, 1248 s, 1296 s (double), 1350 av, 1380 s, 1439 vs, 1638 av, 1663 s, 1708 av cm^{-1}.

For the 4th fraction were found:

d^{20}_4 1.0642, $n^{20}D$ 1.4920, MR 48.82; calc. 47.96. Found %: C 54.39, 54.35; H 6.40, 6.48; Cl 39.29, 39.47. $C_8H_{12}Cl_2$. Calculated %: C 53.65; H 6.73; Cl 39.60.

IR spectrum: 769, 822 av, 846 av (?), 875 w, 929 av, 966 vs, 1009 av, 1067, 1108 s, 1160 av, 1197 av, 1218 w, 1250 s, 1283 av (double), 1351 w, 1383 s, 1443 vs, 1639 w, 1664 s, 1712 w cm^{-1}.

After 100 hours, the fraction reacted to 78.2 and 78.1% with urotropin. 1.52 and 1.60 double bonds were found by Kaufmann's method.

The aldehyde obtained by the Sommelet reaction on the 4th fraction (7-chlorooctadien-2,6-al) was a colorless oil with a characteristic, unpleasant smell.

B.p. 107-109° (10 mm), d^{20}_4 1.0391, $n^{20}D$ 1.4970, MR 44.67; calc. 43.09. Found %: C 60.31, 60.86; H 7.01, 7.40; Cl 22.52, 22.71. $C_8H_{11}OCl$. Calculated %: C 60.57; H 6.99; Cl 22.35.

IR spectrum: 763 av, 788 s, 973 s, 1010 s, 1098 s, 1130 s, 1175 av, 1211 w, 1242 w, 1285 av, 1300 w, 1340 w, 1379 av, 1430 s, 1635 s, 1685 vs cm^{-1}.

2,4-Dinitrophenylhydrazone: m.p. 147-148° (from alcohol).

Found %: N 16.72, 16.56. $C_{14}H_{15}O_4N_4Cl$. Calculated %: N 16.54.

The residue from the Sommelet reaction had b.p. 80-90° (10 mm), d^{20}_4 1.0570, $n^{20}D$ 1.4808.

Found %: C 53.89, 54.01; H 7.22, 7.20; Cl 37.97, 37.68. $C_8H_{12}Cl_2$. Calculated %: C 53.65; H 6.73; Cl 39.60.

IR Spectrum: 768, 787, 820 av, 873 w, 927 vs, 933 s, 1013 w, 1071 s, 1147 av, 1160 w, 1183 av, 1221 av, 1239 av, 1296 av (double), 1350 w, 1380 s, 1440 vs, 1632 av, 1657 av, 1711 s cm^{-1}.

The aldehyde obtained from the 2nd fraction by the Sommelet reaction had the same infrared spectrum and gave with 2,4-dinitrophenylhydrazine a crystalline derivative with the same melting point as the aldehyde from the 4th fraction. The residue from the Sommelet reaction had b.p. 80-85° (10 mm), d^{20}_4 1.0463, $n^{20}D$ 1.4794.

Found %: Cl 36.87, 36.52. $C_8H_{12}Cl_2$. Calculated %: Cl 39.60.

IR spectrum: 763 av, 787 s, 876 w, 927 s, 987 av, 1013 w, 1072 s, 1147 av, 1162 w, 1183 av, 1221 av, 1237 av, 1296 av (double), 1350 w, 1380 s, 1445 vs, 1660 av, 1710 av cm^{-1}.

When 13.7 g of the whole telomer $C_8H_{12}Cl_2$ (fraction 89-102° at 10 mm) was hydrogenated over 23 g of Pd / $CaCO_3$ 5200 ml of hydrogen (758 mm, 21°) was absorbed and this corresponds to 68%, calculated on 4 moles of hydrogen per mole of chloride. The solution was found to contain 4.538 g of chloride ion, which corresponds to 83.7%. On steam distillation and salting out with $CaCl_2$, the reaction mixture yielded n-octane (3.7 g) with b.p. 124-125.5°, d^{20}_4 0.7058, $n^{20}D$ 1.3990, which are close to literature data [9]. The infrared spectrum did not differ from that presented for n-octane in a previous communication. Only the frequency at 1132 cm^{-1} had a higher intensity for an unknown reason.

In the experiment in which anhydrous ferric chloride was used as catalyst under conditions corresponding exactly to those reported by A. L. Klebanskii and his co-workers, from 125 g of dichlorobutene and 23 g of butadiene we obtained a total of 2.2 g of a fraction with b.p. 75-95° (10 mm), d^{20}_4 1.0960, and $n^{20}D$ 1.4852 [and 2.5 g of residue].

Found %: C 45.48, 45.61; H 6.32, 6.37; Cl 37.56, 37.65. $C_8H_{12}Cl_2$. Calculated %: C 53.65; H 6.73; Cl 39.60.

IR spectrum: 768 av, 784 w, 823 av, 930 s, 987 av, 1018 w, 1059, 1072 av, 1100 s, 1142 w, 1164 av, 1191 av, 1223 av, 1253 s, 1283, 1301 av, 1357 av, 1385 s, 1439 vs, 1662 s,/1711s cm^{-1}.

2,4-Dinitrophenylhydrazone: m.p. 133-135° (from alcohol).

Found %: N 18.64, 18.80. $C_{14}H_{17}O_4N_4Cl$. Calculated %: N 16.44.

The infrared spectra were plotted on an IKS-14 spectrophotometer with a NaCl prism and a layer thickness of 0.032 mm. In addition, the regions around 1.6 μ were investigated with a glass prism and a thick layer.

SUMMARY

1. It was shown that contrary to the data of A. L. Klebanskii, A. G. Sayadyan,and M. G. Barkhudaryan, in the telomerization of butadiene with 1,3-dichlorobutene-2, not only 1,4-addition occurred, but also 1,2.

2. It was established that in contrast to crotoyl chloride, 1,3-dichlorobutene-2 did not add to butadiene in noticeable amounts in the form of its allyl isomer.

3. The aldehyde 7-chlorooctadien-2,6-al was obtained from the 1,4-adduct by the Sommelet reaction.

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STUDY OF THE CONVERSIONS OF β-GLYCOLS OF THE ACETYLENE SERIES

II. STUDY OF THE CONVERSIONS OF 3,5-DIMETHYLHEXYNE-1-DIOL-3,5 AND 4,6-DIMETHYLHEPTYNE-2-DIOL-4,6

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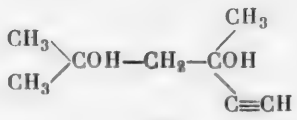
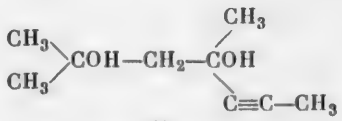
One of us and L. A. Pavlova studied the conversions of the acetylene β-glycol 2,4-dimethyl-6-phenylhexyne-5-diol-2,4 under the action of aqueous and alcohol solutions of sulfuric acid of various concentrations [1] and it was shown that under these conditions the dehydration of this glycol occurred with the formation of the enyne alcohol 2,4-dimethyl-6-phenylhexen-3-yn-5-ol-2, which then decomposed to acetone and isopropenylphenylacetylene.

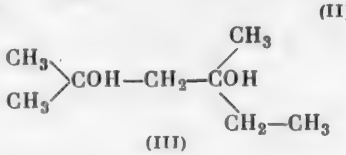
It was interesting to determine whether this conversion was general for acetylene β-glycols of similar structure. For this purpose we synthesized and studied the glycols 3,5-dimethylhexyne-1-diol-3,5 (I) and 4,6-dimethylheptyne-2-diol-4,6 (II) and also the saturated analog of the first glycol, 2,4-dimethylhexanediol-2,4 (III).



(I)

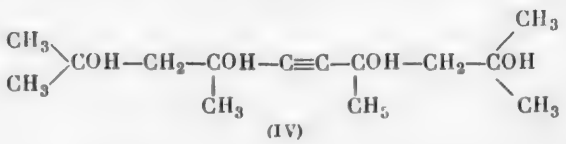


(II)



(III)

Glycol (I) was synthesized by Iotsich's method from diacetone alcohol and acetylenedimagnesium dibromide. As a side product we obtained the erythritol 2,4,7,9-tetramethyldecyne-5-tetraol-2,4,7,9 (IV).

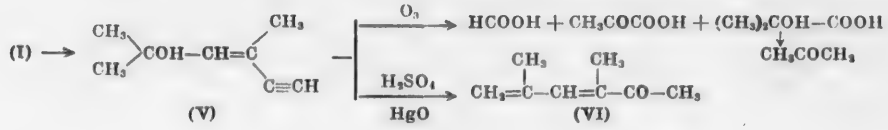


(IV)

With respect to an ammoniacal solution of silver oxide, the glycol (I) obtained behaved similarly to the acetylene γ-glycol 3-methylhexyne-1-diol-3,6, which was prepared previously by one of us together with O. V. Sergievskaya [2]. Both of the glycols gave precipitates of silver acetylide only on heating with the silver reagent. The results of elementary analysis of glycol (I) corresponded to the formula given, but determination of the number of hydroxyl groups by Terent'ev's method gave somewhat low results. The infrared spectrum of the glycol, plotted in the regions of 2900-3650 cm^{-1} with an LiF prism and a layer thickness of 3μ, confirmed the presence of

associated hydroxyls, as shown by a very intense, broad absorption band over the range 3100-3500 cm^{-1}. The infrared spectrum of glycol (I) was also plotted over the range 2000-2200 cm^{-1} with an LiF prism and a layer thickness of 200 μ. A sharply expressed, single absorption maximum at the frequency 2099 cm^{-1} corresponded to a triple bond with a free acetylene hydrogen.

The structure of glycol (I) was confirmed by its decomposition to diacetone alcohol and acetylene when heated with an aqueous solution of potassium hydroxide. The conversions of the glycol obtained under various conditions were studied. Thus, when treated with 0.1 N hydrochloric acid, it was dehydrated to form enyne alcohol (V), which reacted with an ammoniacal solution of silver oxide in the cold.

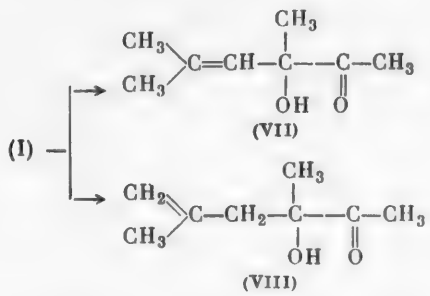


Under the conditions studied, the yield of alcohol (V) did not exceed 18% and the bulk of the glycol was recovered unchanged. The structure of alcohol (V) was demonstrated by ozonization and hydration by Kucherov's method.

The ozonolysis products yielded formic acid, which was determined by Fincke's method [3], pyruvic acid, characterized as the 2,4-dinitrophenylhydrazone, which did not depress the melting point of an authentic sample, and a very small amount of acetone, which could have been formed by further oxidation of the α-hydroxyisobutyric acid.

Hydration of alcohol (V) yielded diene ketone (VI) as a result of hydration and dehydration of the enyne alcohol, as was confirmed by analysis of the 2,4-dinitrophenylhydrazone obtained from ketone (VI).

Hydration of glycol (I) by Kucherov's method was accompanied by its dehydration so that we obtained isomeric keto alcohols, which gave 2,4-dinitrophenylhydrazones of a yellow and a red color. Since the molecular refractions found for the two keto alcohols agreed very well with those calculated theoretically, the double bonds in the molecules of these compounds must have been isolated and the dehydration must have occurred at the expense of the hydroxyl group adjacent to the two methyl groups.



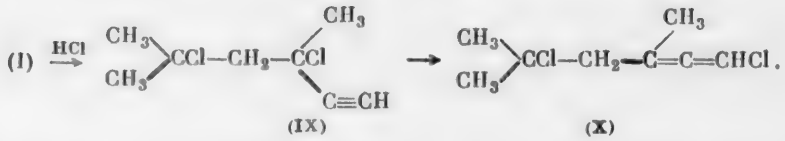
Normally, the dehydration of acetylene glycols occurs at the expense of the hydroxyl adjacent to the triple bond; the liberation of water at the expense of the other hydroxyl in the case of glycol (I) may be explained by the fact that hydration of the triple bond occurred first and then the water was liberated.

The small amounts of the keto alcohols 2,4-dimethylhexen-2-ol-4-one-5 and 2,4-dimethylhexen-1-ol-4-one-5 obtained made it impossible to determine which of them corresponded to Formula (VII) and which to (VIII).

By comparing the results of the interaction of glycol (I) and 2,4-dimethyl-6-phenylhexyne-5-diol-2,4 [1] with acids, we see that in this and in the other case dehydration of the glycols occurs at the expense of the hydroxyl adjacent to the triple bond with the formation of the corresponding enyne alcohols. The enyne alcohol from glycol (I) was stable under the reaction conditions and did not undergo ketonic cleavage in contrast to the other enyne alcohol, which could be isolated only under mild conditions by a reaction with an alcohol solution of sulfuric acid.

We previously observed [4] ketonic decomposition of phenyl-containing ethylene alcohols: 2-phenylpenten-4-ol-2 decomposes in an acid medium to propylene and acetophenone (27%). In the ketonic cleavage of diphenylallylcarbinol, the yield of benzophenone was 73%.

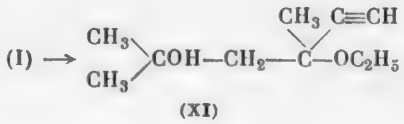
As was said above, glycol (I) reacted with an ammoniacal solution of silver oxide only on heating, while enyne alcohol (V) reacted with this reagent in the cold. It was interesting to determine whether the dichloride obtained by replacing both hydroxyls in the glycol by chlorine atoms would react with the silver reagent. For this purpose, glycol (I) was treated with concentrated hydrochloric acid in the cold. The dichloride obtained gradually lost hydrogen chloride, since even the freshly distilled product gave low results on analysis for chlorine. Dichloride (IX) did not react with an ammoniacal solution of silver oxide under any conditions and did not react with methylmagnesium iodide either. The absence of a triple bond from the dichloride was confirmed by plotting an infrared spectrum in the region of 2000-2100 cm^{-1}, using an LiF prism, since the absorption maximum characteristic of a triple bond was absent from this region and this compelled us to assume that the dichloride underwent an acetylene–allene rearrangement under the reaction conditions.



(IX) (X)

To confirm the structure of dichloride (X), we plotted its infrared spectrum in the region of 1900-2100 cm^{-1}, when an intense absorption band was observed at 1958 cm^{-1}; this maximum may be assigned with high probability to the characteristic frequency of the allene structure [5].

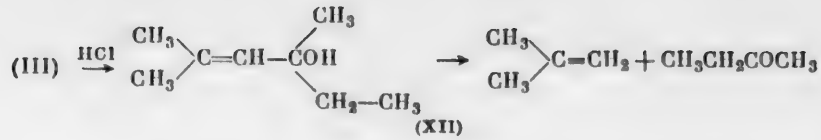
We made a systematic study of the interaction of acetylene alcohols and glycols with sodium and halogen derivatives in a liquid ammonia medium. In a previous communication it was shown that the reaction of dimethylacetylenylcarbinol with sodium and ethyl and benzene bromides formed the corresponding ethers [6]. The reaction of glycol (I) with sodium and ethyl bromide might have been expected to form two isomeric monoethers and the replacement of the acetylene hydrogen by sodium and then ethyl was also possible. The monoether (XI) of the acetylene glycol, obtained by this reaction, was formed at the expense of the hydroxyl adjacent to the triple bond, since when the ether was heated with an aqueous solution of alkali, it was not cleaved to acetylene and the ethyl ether of diacetone alcohol as would have occurred had there been a free hydroxyl in the ether next to the triple bond.



(XI)

The infrared spectrum of the monoether was plotted in the region of 2000-2200 cm^{-1} with an LiF prism. The absorption maximum corresponded to 2096 cm^{-1}, i.e., the characteristic frequency of valence oscillations of an acetylene group with a free hydrogen atom.

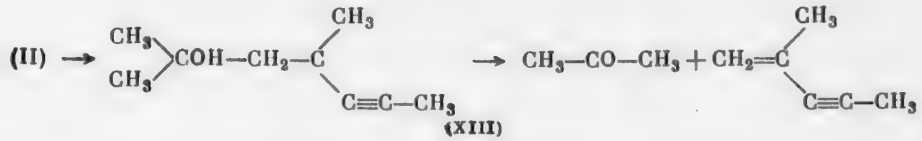
To compare the properties of acetylene glycol (I) and the saturated glycol with the same carbon skeleton, we prepared 2,4-dimethylhexanediol-2,4 (III) from ethylmagnesium bromide and diacetone alcohol and treated it with 0.1 N hydrochloric acid. The reaction products yielded an ethylene alcohol, 2,4-dimethylhexen-2-ol-4 (XII) and its cleavage products: methyl ethyl ketone and an unsaturated hydrocarbon, which in all probability was isobutylene. In addition to methyl ethyl ketone, cleavage of the glycol should have yielded trimethylcarbinol, the dehydration of which could have formed isobutylene. Thus, the properties of the saturated glycol were found to be analogous to those of the glycol with a phenylacetylene radical.



(XII)

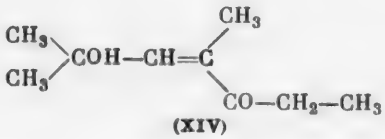
As a second acetylene glycol we took glycol (II), in which the acetylene hydrogen is replaced by a methyl radical. It was synthesized from diacetone alcohol and methylacetylenemagnesium bromide; when hydrogenated, it absorbed the amount of hydrogen calculated for a triple bond.

When glycol (II) was treated with 10% sulfuric acid, on one hand, the reaction proceeded completely analogously to that with the glycol with a phenylacetylene radical [1]: the glycol was first dehydrated to form 4,6-dimethylhepten-4-yn-2-ol-6 (XIII) and then the enyne alcohol decomposed to acetone and methylisopropenylacetylene.



(XIII)

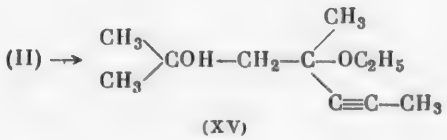
On the other hand, the reaction products yielded an unsaturated keto alcohol, the product of dehydration and hydration of the glycol. Since the molecular refraction obtained for this alcohol showed considerable exaltation in comparison with the theoretically calculated value, there must have been a conjugated system of double bonds in the molecule of this alcohol and its structure must have corresponded to 2,4-dimethylhepten-3-ol-2-one-5 (XIV).



(XIV)

As stated above, we observed simultaneous hydration and dehydration in the reaction of glycol (I) with sulfuric acid and mercuric oxide. Here the same hydration proceeded extremely readily in the absence of mercuric oxide and with only 10% sulfuric acid.

In the interaction of glycol (II) with sodium and ethyl bromide in a liquid ammonia medium, the reaction proceeded analogously to that with glycol (I): the monoether (XV) of the glycol was formed at the expense of the hydroxyl adjacent to the triple bond.



(XV)

When ether (XV) was heated with a 10% solution of potassium hydroxide only traces of methylacetylene were liberated due to the possible traces of the original glycol, while the ether itself was recovered unchanged.

On comparing the properties of all four β-glycols obtained from diacetone alcohol, it can be stated that only glycol (I) with a free acetylene hydrogen gives an enyne alcohol in an acid medium, which did not decompose under these conditions to a ketone and a hydrocarbon. The enyne alcohols formed by dehydration of the glycols with phenylacetylene and methylacetylene radicals decomposed especially readily and the dehydration product of the saturated glycol decomposed with considerably more difficulty.

The triple bond in the glycol containing a methylacetylene radical was hydrated most readily.

EXPERIMENTAL

3,5-Dimethylhexyne-1-diol-3,5 (I)

Synthesis of 3,5-dimethylhexyne-1-diol-3,5. The glycol was prepared by Iotsich's method from diacetone alcohol (1 mole) and acetylenedimagnesium dibromide (2 moles). After decomposition of the organomagnesium complex with water and sulfuric acid (1:5), the reaction product was extracted with ether and the extracts dried with magnesium sulfate. The diol could not be dried with potassium carbonate since in the presence of very small traces of potassium carbonate, the glycol decomposed on distillation of diacetone alcohol and acetylene. The yield of glycol was 25 g (25%); in addition, we obtained the erythritol (IV) in about 5% yield.

3,5-Dimethylhexyne-4-diol-3,5 was a thick liquid, which rapidly turned yellow and did not crystallize on standing.

B.p. 120-121° (28 mm), 86° (3 mm), $n^{20}D$ 1.4535, d^{20}_4 0.9618, MR_D 39.95. $C_8H_{14}O_2$ F. Calculated 40.20.

Found %: C 67.43; H 9.92; number of H_{act} 1.7. M 175. $C_8H_{14}O_2$. Calculated %: C 67.60; H 9.86; number of H_{act} 2. M 142.

The glycol reacted with an ammoniacal solution of silver oxide on heating, when the reaction mixture darkened, became turbid and brown and then lightened as heating continued and a greyish precipitate formed, which exploded on drying.

On distillation of glycol (I), the erythritol (IV) remained in the distillation flask as a thick brown mass; when washed with ether, it crystallized as fine, white crystals, which were recrystallized from alcohol to give thick, clear, colorless platelets, 0.5 cm along the side of the square. The melting point of 2,4,7,9-tetramethyldecyne-5-tetraol-2,4,7,9 was 121-122°.

Found %: C 65.05; H 10.01. $C_{14}H_{26}O_4$. Calculated %: C 65.10; H 10.07.

Decomposition of glycol (I) in an alkaline medium [7]. 5 g of glycol, 1 g of potassium hydroxide and 5 ml of water were slowly distilled and the acetylene passed through ILosvay's solution (meat red precipitate); the distillate contained acetone, which was identified as its 2,4-dinitrophenylhydrazone. The diacetone alcohol obtained by decomposition of the glycol decomposed to acetone in an alkaline medium.

Interaction of 3,5-dimethylhexyne-1-diol-3,5 with hydrochloric acid. 10 g of glycol, 5 ml of 0.5 N hydrochloric acid and 60 ml of water were distilled. The level of the liquid in the distillation flask was kept constant by the addition of water from a dropping funnel. The distillate obtained was extracted with ether, the extract dried with Na_2SO_4, the ether removed and the residue distilled at 25-18 mm. The 1st fraction had b.p. 61-67° (25 mm), 1.6 g (18%); 2nd fraction 112-113° (18 mm), 4 g (original glycol). The bulk of the glycol was extracted from the residue in the distillation flask.

The 1st fraction was the enyne alcohol 3,5-dimethylhexen-3-yn-1-ol-5 (V), gave a precipitate of the silver derivative and reacted with CH_3MgI and $KMnO_4$. The product accumulated from several experiments was vacuum distilled.

B.p. 62-65° (30 mm), $n^{20}D$ 1.4580, d^{20}_4 0.8882, MR_D 38.11. $C_8H_{12}O$ F F. Calculated 38.10.

Found %: C 76.44; H 9.70; number of H_{act} 1.06. M 115. $C_8H_{12}O$. Calculated %: C 77.40; H 9.67; number of H_{act} 1.0. M 124.

Ozonization of enyne alcohol (V). 1.8 g of alcohol was ozonized and about 100% of ozone was absorbed. The ozonide was decomposed with sodium carbonate solution. The neutral products were distilled into a solution of 2,4-dinitrophenylhydrazine. The 2,4-dinitrophenylhydrazone obtained did not depress the melting point of authentic acetone 2,4-dinitrophenylhydrazone. The solution of salts was evaporated and acidified with dilute sulfuric acid and the formic acid was then distilled (formation of a precipitate with calomel). The involatile acids were extracted on an extractor. After removal of the ether, the residue was treated with a solution of 2,4-dinitrophenylhydrazine and the light yellow precipitate obtained was recrystallized from glacial acetic acid; the m.p. was 206°. A mixed melting point with authentic pyruvic acid 2,4-dinitrophenylhydrazone was not depressed.

Hydration of 3,5-dimethylhexen-3-yn-1-ol-5 (V). 2.1 g of enyne alcohol, 0.21 g of mercuric oxide, 1.25 ml of sulfuric acid and 8 ml of water were stirred in the cold for 40 minutes and then the reaction mixture was diluted with twice its volume of water and steam distilled. The distillate was extracted with ether, the extract dried with sodium sulfate, the ether removed and the residue distilled at 18 mm.

The 1st fraction had b.p. 52-62°, 0.3 g; 2nd fraction 62-65°, 0.2 g. The 2nd fraction and the residue in the distillation flask gave a bright red precipitate with a solution of 2,4-dinitrophenylhydrazine with m.p. 195-197° (from alcohol). A mixed melting point with authentic mesityl oxide 2,4-dinitrophenylhydrazone was not depressed.

Found %: N 18.50. $C_{14}H_{16}O_4N_4$. Calculated %: N 18.42.

Hydration of 3,5-dimethylhexyne-1-diol-3,5 (I) was carried out under the same conditions as the hydration of the enyne alcohol. From the reaction products we isolated two unsaturated keto alcohols, 2,4-dimethylhexen-2-ol-4-one-5 and 2,4-dimethylhexen-1-ol-4-one-5 (VII) and (VIII), formed due to hydration and dehydration of the glycol.

1) B.p. 68-72° (32 mm), $n^{20}D$ 1.4255, d^{20}_4 0.9236, MR_D 40.45. $C_8H_{14}O_2$ F. Calculated 40.21. Found M 146; calc. 142.

2) B.p. 82° (20 mm), $n^{20}D$ 1.4570, d^{20}_4 0.9551, MR_D 40.05. $C_8H_{14}O_2$ F. Calculated 40.21. Found M 144; calc. 142.

The two substances had pleasant smells, rapidly decolorized $KMnO_4$ solution, and formed a precipitate with 2,4-dinitrophenylhydrazine solution, the first one yellow with m.p. 187° (from alcohol) and the second, red with m.p. 160° (from alcohol).

2,4-Dinitrophenylhydrazone with m.p. 187°. Found %: C 51.94; H 5.76; N 17.42. $C_{14}H_{18}O_5N_4$. Calculated %: C 52.17; H 5.59; N 17.39.

2,4-Dinitrophenylhydrazone with m.p. 160°. Found %: N 17.45. $C_{14}H_{18}O_5N_4$. Calculated %: N 17.39.

Interaction of 3,5-dimethylhexyne-1-diol-3,5 with concentrated hydrochloric acid. 20 g of the glycol was rapidly added to 120 ml of 37% hydrochloric acid. The mixture was stirred vigorously for 1 hour. The very dark reaction products were diluted with ether. The ether layer was separated and dried with potassium carbonate. After removal of the ether, the residue was vacuum distilled. The 1st fraction had b.p. 42-45° (1 mm), 0.5 g, $n^{20}D$ 1.4770; 2nd fraction 45-50° (1 mm), 6 g, $n^{20}D$ 1.4845.

Redistillation of the second fraction yielded a few drops of a liquid with b.p. 42-45° (1 mm), $n^{20}D$ 1.4840, and 5 g of the allene dichloride 3,5-dimethyl-1,5-dichlorohexadiene-1,2 (X).

B.p. 45-48° (1 mm), $n^{20}D$ 1.4860, d^{20}_4 1.0689, MR_D 48.05. $C_8H_{12}Cl_2$ F_2. Calculated 48.04.

Freshly distilled dichloride. Found %: Cl 35.54. $C_8H_{12}Cl_2$. Calculated %: Cl 39.67.

Chloride on the next day after distillation. Found %: Cl 34.42.

Interaction of 3,5-dimethylhexyn-1-diol-3,5 with sodium and ethyl bromide in liquid ammonia. 18 g of glycol (I) was placed in a large, wide test tube with liquid ammonia. The tube was cooled with carbon dioxide and ether to −60-40°. An equivalent amount of metallic sodium (calculated on a monosubstituted derivative of the glycol) was added in small pieces while the reaction mixture was stirred and then an amount of ethyl bromide was added equivalent to the sodium taken. Stirring was continued for a further 2 hours and then absolute ether was introduced into the tube. The ammonia evaporated overnight. The ether solution was filtered from the NaBr precipitate, the ether removed and the residue distilled at 65 mm. The first fraction had b.p. 101-108°, 2.5 g, $n^{20}D$ 1.4362; 2nd fraction 108-116°, 10 g, $n^{20}D$ 1.4375.

Both fractions had a sharp camphor-like smell, did not give a precipitate with an ammoniacal solution of silver oxide, decolorized $KMnO_4$ solution and reacted with CH_3MgI. The residue in the flask was distilled at 3 mm. The b.p. was 86-90° and $n^{20}D$ 1.4530, which corresponds to the original glycol.

The first two fractions were combined and distilled at 45 mm. Fractions were obtained: 1st 95-102°, 2.2 g, $n^{20}D$ 1.4360; 2nd 102-106°, 2.8 g, $n^{20}D$ 1.4360; 3rd 106-108°, 6.5 g, $n^{20}D$ 1.4370. The residue in the flask was about 1 g and had $n^{20}D$ 1.4480. All the fractions were the same substance, (XI), slightly contaminated with the original glycol.

B.p. 95-102° (45 mm), $n^{20}D$ 1.4360, d^{20}_4 0.8950, MR_D 49.66. $C_{10}H_{18}O_2$ F. Calculated 49.55.

Found %: C 70.52; H 11.28; number of H_{act} 0.79. $C_{10}H_{18}O_2$. Calculated %: C 70.59; H 10.60; number of H_{act}. 1.

The acetylene monoether (XI) obtained, 3,5-dimethyl-3-ethoxyhexyn-1-ol-5 did not give a precipitate with an ammoniacal solution of silver oxide even on heating.

Interaction of monoether (XI) of the glycol with alkali. 6 g of the glycol ether was heated with 20% potassium hydroxide solution. The acetylene liberated was very little and was apparently caused by a very small amount of the original glycol in the monoether. The substance isolated from the alkaline solution had the same constants as the monoether.

Interaction of the glycol monoether with 0.5 N sulfuric acid. When 5 g of the monoether was distilled with 50 ml of 0.5 N sulfuric acid, the expected dehydration did not occur.

2,4-Dimethylhexanediol-2,4 (III)

2,4-Dimethylhexanediol-2,4 was prepared from diacetone alcohol and ethylmagnesium bromide in 58% yield.

B.p. 109-109.5° (16 mm), $n^{20}D$ 1.4418, d^{20}_4 0.9241, MR_D 41.80. $C_8H_{18}O_2$. Calculated 42.19.

Literature data [8]: b.p. 99-100° (5 mm), $n^{20}D$ 1.4417, d^{20}_4 0.9215.

Interaction of 2,4-dimethylhexanediol-2,4 with hydrochloric acid. 20 g of glycol and 75 ml of 0.1 N hydrochloric acid were heated below the boiling point for 1.5 hours; a very small amount of gas was liberated through the reflux condenser and this had a hydrocarbon-like smell and decolorized a solution of potassium permanganate. The upper layer was separated and the aqueous one saturated with potassium carbonate and extracted with ether. After removal of the ether, the products isolated were distilled at atmospheric pressure. The 1st fraction had b.p. 82-93°, 1 g of methyl ethyl ketone; 2nd fraction 93-123°, 1.5 g; 3rd fraction 123-154°, a few drops; 4th fraction 154-155°, 7 g.

The 1st fraction gave a 2,4-dinitrophenylhydrazone with m.p. 111-112°; a mixed melting point with authentic methyl ethyl ketone 2,4-dinitrophenylhydrazone was not depressed. The 3rd fraction gave a red 2,4-dinitrophenylhydrazone with m.p. 197° (from alcohol). A mixed melting point with a 2,4-dinitrophenylhydrazone of mesityl oxide was not depressed. The mesityl oxide could have been formed from diacetone alcohol, which may have been present in the original glycol.

The 4th fraction corresponded to 2,4-dimethylhexen-2-one-4 (XII).

B.p. 154-155°, $n^{20}D$ 1.4442, d^{20}_4 0.8574, MR_D 39.70. $C_8H_{16}O$ F. Calculated 40.20.

Literature data [9]: b.p. 48-50° (3-6 mm), $n^{17}D$ 1.4460, d^{17}_4 0.8600.

4,6-Dimethylheptyne-2-diol-4,6 (II)

4,6-Dimethylheptyne-2-diol-4,6 was synthesized by Iotsich's method from diacetone alcohol and methyl acetylenemagnesium bromide in 40% yield as a thick, colorless, uncrystallizable liquid.

B.p. 118-122° (16 mm), $n^{20}D$ 1.4532, d^{20}_4 0.9363, MR_D 45.05. $C_9H_{16}O_2$ F. Calculated 44.81.

Found %: C 69.32; H 10.10; number of H_{act} 1.56. $C_9H_{16}O_2$. Calculated %: C 69.23; H 10.25; number of H_{act}. 2.

The low result obtained on determining the number of active hydrogen atoms may be explained by the presence of hydrogen bonds, as was the case with glycol (I).

Hydrogenation of 4,6-dimethylheptyne-2-diol-4,6. 3 g of glycol was hydrogenated over platinum black. 84% of the theoretical amount of hydrogen for a triple bond was absorbed. Removal of the solvent yielded 1.3 g of the saturated glycol 2,4-dimethylheptanediol-2,4.

B.p. 106-107 (10 mm), $n^{20}D$ 1.4412, d^{20}_4 0.9110, MR_D 46.42; calc. 46.92.

Found %: C 66.94; H 12.39. $C_9H_{20}O_2$. Calculated %: C 67.50; H 12.50.

Interaction of 4,6-dimethylheptyne-2-diol-4,6 with 10% sulfuric acid. 6.9 g of diol (III) was stirred and heated with 70 ml of 10% sulfuric acid on a boiling water bath for 2 hours. The reaction mixture was extracted with ether and the ether extract washed with sodium carbonate solution and water and dried with potassium carbonate. After removal of the ether, the residue was distilled at atmospheric pressure; we obtained about 1 g of hydrocarbon, methylisopropenylacetylene.

B.p. 92-94°, $n^{20}D$ 1.4429, d^{20}_4 0.7522, MR_D 28.15. C_6H_7 F. Calculated 27.44.

Found %: C 90.15; H 10.00. C_6H_8. Calculated %: C 90.00; H 10.00.

The acid aqueous solution left after the ether extraction was steam distilled. The first drops of the distillate were collected in a solution of 2,4-dinitrophenylhydrazine. The precipitate obtained had m.p. 124° (from alcohol); a mixed melting point with authentic acetone 2,4-dinitrophenylhydrazone was not depressed. The residue in the distillation flask was extracted with ether and the extract dried with potassium carbonate; the ether was removed and the residue vacuum distilled. The yield was 1 g.

B.p. 109-113° (20 mm), $n^{20}D$ 1.4588, d^{20}_4 0.9188, MR_D 46.39. $C_9H_{16}O_2$ F. Calc. 44.83.

Found %: C 68.03; H 11.05; number of H_{act} 1.02. $C_9H_{16}O_2$. Calculated %: C 69.23; H 10.25; number of H_{act} 1.

The unsaturated keto alcohol obtained, 2,4-dimethylhepten-3-ol-2-one-5 (XIV), was converted into a 2,4-dinitrophenylhydrazone with m.p. 156-157°

Found %: C 53.65; H 6.06; N 16.61. $C_{15}H_{20}O_5N_4$. Calculated %: C 53.93; H 5.98; N 16.67.

Reaction of 4,6-dimethylheptyne-2-diol-4,6 with sodium and ethyl bromide in liquid ammonia was carried out under the conditions described for 3,5-dimethylhexyne-1-diol-3,5. The monoether (XV), 4,6-dimethyl-4-ethoxyheptyn-2-ol-6, was obtained in 60% yield.

B.p. 97-101° (22 mm), $n^{20}D$ 1.4361, d^{20}_4 0.8909, MR_D 54.02. $C_{11}H_{20}O_2$ F. Calculated 54.17.

Found %: C 70.48; H 11.50; OC_2H_5 25.72; number of H_{act} 1.21. M 174. $C_{11}H_{20}O_2$. Calculated %: C 71.73; H 10.87; OC_2H_5 25.46; number of H_{act} 1. M 184.

Action of alkali solution on 4,6-dimethyl-4-ethoxyheptyn-2-ol-6. 6 g of the glycol monoether was boiled with 65 ml of 10% potassium hydroxide solution for 2 hours. The reaction products yielded 4 g of the original substance with b.p. 98-99° (20 mm) and $n^{20}D$ 1.4370. The liberation of methylacetylene was not observed.

SUMMARY

1. A study was made of the conversions of three glycols: 3,5-dimethylhexyne-1-diol-3,5; 4,6-dimethylheptyne-2-diol-4,6; and 2,4-dimethylhexanediol-2,4.

2. It was shown that on interaction with dilute hydrochloric and sulfuric acids, 3,5-dimethylhexyne-1-diol-3,5 was dehydrated with the formation of the enyne alcohol 3,5-dimethylhexen-3-yn-1-ol-5.

3. The interaction of 3,5-dimethylhexyne-1-diol-3,5 and 4,6-dimethylheptyne-2-diol-4,6 with sodium and ethyl bromide in liquid ammonia yielded monoethyl ethers of the glycols, 3,5-dimethyl-3-ethoxyhexyn-1-ol-5 and 4,6-dimethyl-4-ethoxyheptyn-2-ol-6, at the expense of the hydroxyl adjacent to the triple bond. The first ether did not give a precipitate with an ammoniacal solution of silver oxide even on heating, in contrast to the glycol itself, which gave a precipitate of the acetylide when heated with the silver reagent.

4. The interaction of 3,5-dimethylhexyne-1-diol-3,5 with sulfuric acid in the presence of mercuric oxide resulted in the formation of two isomeric hydration and dehydration products.

5. The interaction of 3,5-dimethylhexyne-1-diol-3,5 with concentrated hydrochloric acid resulted in the formation of a dichloride with an allene structure. Its structure was demonstrated by plotting the infrared spectrum.

6. It was shown that the interaction of the saturated glycol, 2,4-dimethylhexanediol-2,4, with dilute hydrochloric acid produced its dehydration with the formation of the ethylene alcohol, 2,4-dimethylhexene-2-ol, and as a result of the partial decomposition of this, methyl ethyl ketone was liberated.

7. It was shown that in the interaction of the acetylene glycol, 4,6-dimethylheptyne-2-diol-4,6, with dilute sulfuric acid, it was impossible to isolate the corresponding enyne alcohol, which decomposed completely to acetone and methylisopropenylacetylene. In addition, in this reaction we isolated the unsaturated keto alcohol, 2,4-dimethylhepten-3-ol-2-one-5, the product of simultaneous hydration and dehydration.

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INVESTIGATIONS OF THE CHEMISTRY OF CHLOROMYCETIN (LEVOMYCETIN)

IX. SYNTHESIS OF A NEW ANALOG OF CHLOROMYCETIN – D-THREO-1-(p-FORMYLPHENYL) - 2-DICHLOROACETYLAMINO-1,3-PROPANEDIOL

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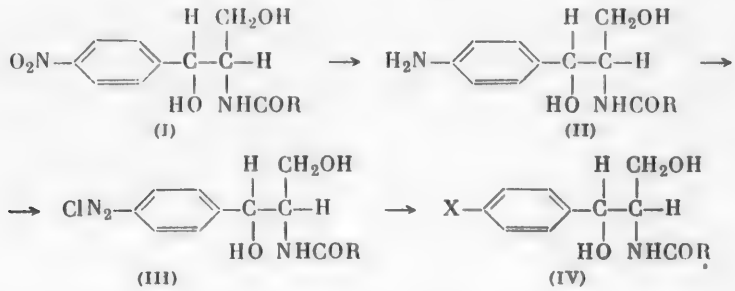
Of the analogs of chloromycetin (chloramphenicol, levomycetin) (I, R = $CHCl_2$), especial consideration is deserved by the previously undescribed D-threo-1-(p-formylphenyl)-2-dichloroacetylamino-1,3-propanediol (IV, X = CHO; R = $CHCl_2$). The presence of the aldehyde group in the molecule offers the possibility of readily synthesizing a considerable number of other, previously inaccessible analogs of chloromycetin, required for further elucidation of various aspects of the relation between structure and antimicrobial activity in this series of compounds [1].

Due to the fact that a few years ago Beech developed a method of introducing an aldehyde group into an aromatic nucleus through the diazo compound [2], the aldehyde interesting us could be synthesized by a simple route, which we proposed [3] for preparing optically active analogs of chloromycetin of the general type (IV, R=$CHCl_2$) directly from chloromycetin itself (I, R=$CHCl_2$).



We first accomplished these conversions, starting not from chloromycetin but from its racemic N-benzoyl analog (I, R=C_6H_5), since it is known that in this case more readily crystallizable compounds are usually obtained. Thus, the diazo group in the compound (III; R=C_6H_5) was replaced by an aldehyde group (by the action of formaldoxime and subsequent hydrolysis with ferric ammonium alum) under conditions close to those recommended [2] as optimal. The D,L-threo-1-(p-formylphenyl)-2-benzoylamino-1,3-propanediol (IV, X=CHO; R=C_6H_5) obtained was readily isolated in a crystalline form due to its capacity to form a readily crystallizable solvate with one molecule of benzene (yield about 15%). This aldehyde was then characterized as the 2,4-dinitrophenylhydrazone, the anil, bisulfite compound and other derivatives.

The preparation of D-threo-1-(p-formylphenyl)-2-dichloroacetylamino-1,3-propanediol (IV, X=CHO; R=$CHCl_2$) was found to be much more difficult. It was synthesized from (III, R=$CHCl_2$) similarly to the previous compound, but we were unable to isolate it in the crystalline state even after careful purification and this aldehyde was characterized as the 2,4-dinitrophenylhydrazone (yield about 12%).

EXPERIMENTAL

1. Preparation of D,L-threo-1-(p-formylphenyl)-2-benzoylamino-1,3-propanediol. 10.6 g of D,L-threo-II ($R=C_6H_5$) was suspended in 50 ml of 12% HCl and diazotized [3] at 0-5° with a solution of 2.6 g of $NaNO_2$ in 5 ml of water (diazotization was complete after 2-3 hours), after which a saturated solution of sodium acetate was added to the solution obtained until the mineral acid reaction disappeared (to Congo). The filtered solution of diazonium salt (III, $R=C_6H_5$) was gradually added with stirring at 10-15° to an aqueous solution of formaldoxime* to which had first been added 25 g of sodium acetate, 1.85 g of copper sulfate and 0.3 g of crystalline sodium sulfite, dissolved in 25 ml of water. The solution of the diazonium salt had to be added under the layer of the liquid. At this, vigorous evolution of nitrogen occurred and a flocculent precipitate formed, which gradually darkened and agglomerated into a lump. Stirring was continued for 1 hour at 10-15°, the mixture was acidified to Congo with concentrated HCl, the solution decanted from the dark, tarry precipitate of the oxime and the latter washed several times with water. The main solution and the wash waters were combined and extracted with ethyl acetate and the extract obtained was washed with sodium bicarbonate solution and then with water and dried with magnesium sulfate. The ethyl acetate was removed in vacuum and the dark, oily residue was added to the water-insoluble oxime precipitate and boiled for 1 hour with a solution of 45 g of ferric ammonium alum in 75 ml of water. The solution was decanted from the tarry residue, the latter boiled many times with small portions of water and the combined aqueous solutions (total volume of about 1 liter) extracted with ether in a liquid extractor for 6 hours. The ether solution was washed with sodium bicarbonate solution and water, then dried with magnesium sulfate and the ether evaporated to a volume of 30-40 ml. An equal amount of benzene was added, the solvent removed almost completely in vacuum and the precipitate collected. We obtained 1.6 g of aldehyde, crystallizing with 1 molecule of benzene. The yield was 15% and the m.p. 84-89° (decomp.) (from benzene).

Found %: C 72.73; H 6.04. $C_{17}H_{17}O_4N \cdot C_6H_6$. Calculated %: C 73.19; H 6.14.

After recrystallization from water, the aldehyde melted at 127-128°.

Found %: C 68.26; H 5.80. $C_{17}H_{17}O_4N$. Calculated %: C 68.19; H 5.72.

The semicarbazone obtained from the aldehyde had m.p. 209-210° (from 20% alcohol) and the 2,4-dinitrophenylhydrazone melted at 212-215° (from a mixture of ethyl acetate and alcohol, 4:1).

2. Preparation of D-threo-1-(p-formylphenyl)-2-dichloroacetylamino-1,3-propanediol. 4.9 g of the hydrochloride of D-threo-II ($R=CHCl_2$) was dissolved in 65 ml of 2.5 %HCl and diazotized over a period of 2-3 hours at 0-5° with a solution of 1.1 g of $NaNO_2$ in 5 ml of water [3]. After the addition of sodium acetate as in the previous case, the filtered solution of the diazonium salt (III, $R=CHCl_2$) was reacted with formaldoxime under the conditions described above. After acidification of the reaction mixture with the concentrated HCl (to Congo), the aqueous solution was decanted from the dark, tarry precipitate** and extracted with ethyl acetate. The extract obtained was washed with sodium bicarbonate solution and water and dried with magnesium sulfate and the ethyl acetate evaporated. The residue was boiled for 1 hour with a solution of 10 g of ferric ammonium alum in 40 ml of water, then extracted with ether, the ether extract washed with sodium bicarbonate solution and water and dried with magnesium sulfate and the ether evaporated. We obtained 0.8 g of a viscous yellow oil, which contained about 70% of aldehyde according to analysis (oximination). If this oil was dissolved in hot water and a solution of 2,4-dinitrophenylhydrazine in 10% HCl added, a gelatinous precipitate of the hydrazone precipitated immediately. To improve the precipitation of the latter, the mixture was heated to boiling and then the precipitate collected, washed with water and dissolved in alcohol with heating. On cooling, the solution deposited a voluminous precipitate of the solvated hydrazone, which was recrystallized from acetic acid. When this solvate was boiled with water, it rapidly lost the solvent molecules; the hydrazone obtained melted at 183-185°.

Found %: C 44.40; H 3.73. $C_{18}H_{17}O_7N_5Cl_2$. Calculated %: C 44.45; H 3.52.

*The solution of formaldoxime was prepared by heating 1.7 g of paraformaldehyde and 3.8 g of hydroxylamine hydrochloride in 25 ml of water until a clear solution was obtained, then 7.5 g of sodium acetate was added and the solution boiled for a further 15 minutes [2].

**It was impossible to isolate the aldehyde from this precipitate either as such or in the form of any derivative.

SUMMARY

A new analog of chloromycetin, D-threo-1-(p-formylphenyl)-2-dichloroacetylamino-1,3-propanediol was synthesized; D,L-threo-(p-formylphenyl)-2-benzoylamino-1,3-propanediol was prepared similarly.

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CATALYTIC OXIDATION OF CYCLOHEXYLAMINE WITH HYDROGEN PEROXIDE TO CYCLOHEXANONE OXIME

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For preparing cyclohexanone oxime, which is used for the production of caprone, it is possible to use the oxidation of cyclohexylamine with hydrogen peroxide in the presence of catalysts. Cyclohexylamine is readily obtained by hydrogenation of aniline.

By the oxidation of various aliphatic amines with Caro's reagent, Bamburger obtained substituted hydroxylamines, nitroso compounds, oximes, ketones and other compounds [1]. Depending on the conditions and the oxidant used, the oxidation of cyclohexylamine can yield cyclohexylhydroxylamine [2], nitrosocyclohexane [3], cyclohexanone oxime [4, 5], cyclohexanone [4, 6] and other products. The use of the following oxidants for cyclohexylamine has been reported: peracetic acid [7], Caro's reagent [1, 3] and hydrogen peroxide [2, 4, 5]. The simplest oxidation is by hydrogen peroxide in the presence of catalysts, salts of uranic, molybdic and tungstic acids, and complexons Trilon B (the disodium salt of ethylenediaminetetraacetic acid) or nitrilotriacetic acid. In this case, the cyclohexylamine is mildly oxidized to cyclohexanone oxime [5].

The problem of the present investigation was to study the oxidation of cyclohexylamine to cyclohexanone oxime with hydrogen peroxide.

EXPERIMENTAL

For the work, we used the following reagents: 98% cyclohexylamine with b.p. 133°, prepared by hydrogenation of aniline, hydrogen peroxide as a 30% aqueous solution, analytical grade ammonium tungstate and analytical grade ammonium molybdate.

The catalyst was dissolved in 0.1 ml of water in a test tube, then 0.17 g of cyclohexylamine was added and hydrogen peroxide was introduced dropwise (drop volume 0.004 ml) with constant shaking over a period of 30-80 minutes. The temperature of the reaction mixture was 30-40°. Due to binding of the cyclohexylamine (pK_B = = 3.35 [8]), the pH of the mixture changed from 11.5 to 9.5 during the reaction.

The cyclohexanone oxime formed during the reaction was determined colorimetrically by a modification of the procedure in [9] with a relative error of ±5% for one experiment.

For the oxidation of cyclohexylamine we tested a series of catalysts forming compounds with hydrogen peroxide: salts of uranic, vanadic, molybdic and tungstic acids. Salts of uranic and vanadic acids were practically inactive. Figure 1 shows the results of oxidizing cyclohexylamine in the presence of salts of molybdic and tungstic acids. Ammonium tungstate in the presence of Trilon B showed the greatest activity. An increase in the effect of ammonium tungstate and molybdate occurred over the range from 0 to 8-12 mg of each catalyst. 8-12 mg of catalyst was equimolecular to the amount of hydrogen peroxide contained in one drop (1.3 g of H_2O_2). With insufficient catalyst with respect to the hydrogen peroxide, the formation of cyclohexanone oxime fell, and with an excess, it did not increase. Consequently, an essential role in the oxidation is played by the interaction of the catalyst with hydrogen peroxide.

It is known that the tungstate ion forms pertungstates with hydrogen peroxide in alkaline solution [10]. On comparing different oxidants reacting with amines, Caro's reagent, peracetic acid and pertungstates, it is obvious

that they all have a peroxide group attached to the acid-forming atoms C, S, W or Mo. Thus, the oxidant is the grouping E−OOH (or EOO^-), where E is the acid-forming atom C, S, W or Mo.

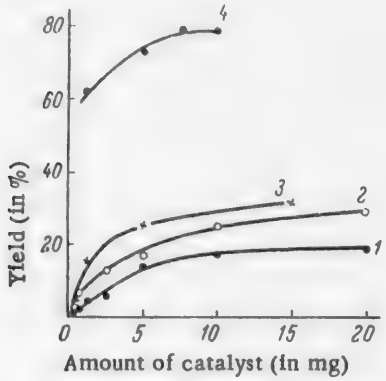

Fig. 1. Yield of cyclohexanone oxime in relation to the amount of catalyst. 1) Ammonium molybdate, 2, 3) ammonium tungstate, 4) ammonium tungstate and 1 mg of Trilon B. In Experiments 1, 2, and 4, 3.4 m moles of hydrogen peroxide was added and in Experiment 3, 5.1 m moles.

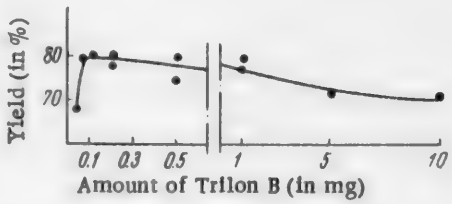

Fig. 2. Yield of cyclohexanone oxime in relation to amount of Trilon B.

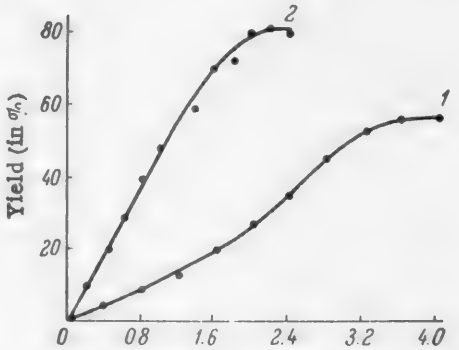

Fig. 3. Yield of cyclohexanone oxime in relation to the amount of hydrogen peroxide. 1) Ammonium tungstate, 2) ammonium tungstate and Trilon B.

Pertungstate was most convenient for the synthesis since as it was consumed in the reaction, it was continually regenerated if excess hydrogen peroxide was available. At the same time, in an alkaline solution peracetic acid and Caro's reagent are irreversibly converted into acetates and sulfates, respectively.

The oxidation of cyclohexylamine with hydrogen peroxide proceeds to the formation of cyclohexanone oxime and side products. A considerable portion (30-60%) of hydrogen peroxide decomposes to oxygen and water. By introducing stabilizers, it was possible to reduce the hydrogen peroxide decomposition to 5% (where Trilon B was used) with a simultaneous increase in the oxime yield. Thus, when 10 mg of stannous chloride was added, the yield of cyclohexanone oxime was 75%, 4 mg of formaldehyde, 75%, 5 mg of phenol, 59% and 0.5 mg of Trilon B, 80%.

The effect of Trilon B concentration on the yield of cyclohexanone oxime is shown in Fig. 2. The experiment was carried out with 10 mg of ammonium tungstate and 3.4 mmole of hydrogen peroxide. Only 0.07 mg of 1/75th of Trilon B relative to the ammonium tungstate was required to suppress the decomposition of hydrogen peroxide to oxygen and water. An increase in the concentration of Trilon B up to equimolecular with the ammonium tungstate hardly affected the yield of cyclohexanone oxime.

This fact and the analogous action on the oxidation of other substances (formaldehyde, phenol and stannous chloride) shows that Trilon B acts as a stabilizer of hydrogen peroxide, suppressing the side reaction of hydrogen peroxide decomposition. The stabilizing action of Trilon B should be ascribed to its capacity to give stable complexes with di- and trivalent cations. Traces of salts of these cations are present in ammonium tungstate. It is worthwhile to remove these traces either by binding them in a stable complex or by extraction with a chloroform solution of dithizone, since the decomposition of hydrogen peroxide is sharply reduced and the yield of oxime increased. Thus, after extraction of traces of cations present in ammonium tungstate, the yield of oxime rose from 30-40 to 70-75%.

With an increase in the amount of hydrogen peroxide added, the yield of oxime increased in the presence of ammonium tungstate along to 58% and with the addition of Trilon B, to 80% with a simultaneous fall in the hydrogen peroxide consumption by a factor of 2 (Fig. 3). The experiments were carried out with 10 mg of ammonium tungstate and 1 mg of Trilon B. Consequently, Trilon B not only protects hydrogen peroxide from decomposition, but also decreases the amount of side products. Decomposition of hydrogen peroxide, catalyzed by traces of heavy metal salts, was accompanied by increased formation of side products. Toward the end of the process, the oxidation of cyclohexylamine proceeded mainly toward the formation of side products, including cyclohexanone, which was identified by reaction with hydroxylamine to form cyclohexanone oxime with m.p. 87-88° (literature data 90° [13]). In the solution we also detected nitrite ion by the formation of a volatile nitrite with methyl alcohol and nitrate ion, which, after removal of the nitrites, was determined colorimetrically by the formation of picric acid with phenolsulfonic acid [11, 12].

SUMMARY

The role of salts of tungstic and molybdic acids and Trilon B in the oxidation of cyclohexylamine was demonstrated.

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INVESTIGATION OF PYRAZOLES

IV. NEW METHOD OF SYNTHESIZING TETRAHYDROINDAZOLES AND INDAZOLES

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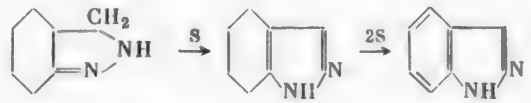
In previous communications, we showed that pyrazolines with alkyl or phenyl substituents in any position in the nucleus were smoothly converted into pyrazoles by dehydrogenation with sulfur [1, 2].

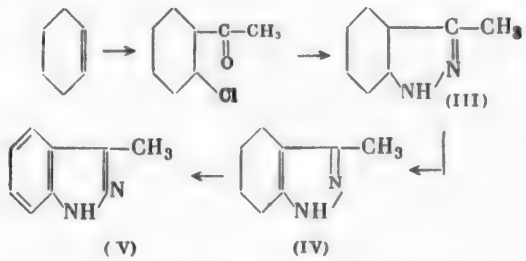
In this work 3,4- and 4,5-tetramethylenepyrazolines were dehydrogenated and it was found that the pyrazoline ring was first dehydrogenated to form 4,5,6,7-tetrahydroindazoles, which were converted to indazoles themselves by further heating with excess sulfur.



(I) (II)

Thus, 3,4-tetramethylenepyrazoline [3] formed 4,5,6,7-tetrahydroindazole (I) in 56% yield and then the indazole itself (II). By dehydrogenation, 3-methyl-4,5-tetramethylenepyrazoline (III) was converted into 3-methyltetrahydroindazole (IV) and 3-methylindazole (V).

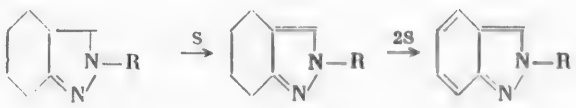
The starting pyrazoline (III) was prepared by the action of acetyl chloride on cyclohexene in the presence of aluminum chloride [4] with subsequent treatment with hydrazine.



(III)

(V) (IV)

A study of the dehydrogenation of 3,4-tetramethylenepyrazolines with substituents in position 1 was of particular interest as in this case one would expect the formation of indazoles with a quinone structure for the nucleus.



The formation of such a structure and its stability under the drastic reaction conditions would have been an indication of quite a high degree of aromaticity of the "quinoid" form of 2-substituted indazoles.

To prepare the starting tetramethylenepyrazolines, substituted in position 1, which have not been described in the literature up to now, we used the reaction of substituted hydrazines with 1-dimethylaminomethylcyclohexanone.

(VI) R = CH_3
(VII) R = $C_6H_5CH_2$
(VIII) R = C_6H_5

By this method we obtained satisfactory yields of 1-methyl- (VI) and 1-benzyl-3,4-tetramethylenepyrazoline (VII). In the case of phenylhydrazine the process proceeded in a very complicated way, giving different reaction products, depending on the conditions. Therefore, we were able to obtain 1-phenyl-3,4-tetramethylenepyrazoline (VIII) in only 21% yield. When these pyrazolines, (VI)-(VIII) were heated with equimolecular amounts of sulfur to 220-270°, the liberation of hydrogen sulfide proceeded smoothly and the corresponding tetrahydroindazoles were formed (in 40-70% yields).

The reaction proceeded over 1-1.5 hours and its end was determined by the cessation of hydrogen sulfide evolution. If the pyrazoline was heated with not one equivalent, but three equivalents of sulfur, then although indazoles were formed, the yields were very small (10-20%) and it was found to be more advantageous to carry out the dehydrogenation in stages: first to tetrahydroindazoles and then the substances isolated were dehydrogenated to indazoles. This method gave pure substances, though the yields remained low (26-35%).

The benzyl derivative (VII) behaved anomalously and when dehydrated completely, it evidently lost the benzyl group and underwent complex conversions.

For characterization, we plotted the ultraviolet absorption spectra. It was found that all the pyrazolines and pyrazoles obtained had an absorption band in the region of 230-240 mμ, which agrees with literature data [2, 5]. When the substituent in position 1 was phenyl, apparently due to conjugation of the bonds of the phenyl nucleus and the indazole nucleus, the maximum was shifted into the longwave region by 30-40 mμ and another maximum appeared in the region of 340-390 mμ, which also agrees with literature data [2]. The values of λ_{max} and log ε are presented in the table.*

Compound	λ_{max}, mμ	lg ε
1-Methyl-3,4-tetramethylenepyrazoline	237	3.60
1-Benzyl-3,4-tetramethylenepyrazoline	240	3.76
1-Phenyl-3,4-tetramethylenepyrazoline	275, 395	4.38, 1.66
Tetrahydroindazole	<220	~3.5
2-Methyltetrahydroindazole	236	3.71
2-Benzyltetrahydroindazole	234	3.85
2-Phenyltetrahydroindazole	272, 336	4.57, 2.45

EXPERIMENTAL

1-Dimethylaminocyclohexanone-2 was obtained by the procedure described previously by one of us [3], but the use of methanol as solvent (40 ml to 1 mole of cyclohexanone) led to more reliable yields.

*The spectra were plotted by V. I. Bogomolova on an SF-4 spectrophotometer; the solvent was methyl alcohol. alcohol.

2-Chlorocyclohexane was synthesized by the procedure reported in the literature [4]. Excess cyclohexane was used as the solvent instead of carbon disulfide and the reaction was carried out at −15°. From 1.2 moles of acetyl chloride and 1.5 moles of cyclohexene we obtained 110 g of a fraction with b.p. 90-110° (9 mm), which was a mixture of 2-chloroacetylcyclohexane and acetylcyclohexene-1. Since both of these compounds gave 3-methyl-4,5-tetramethylenepyrazoline on reaction with hydrazine, the fraction was not resolved into pure components.

1-Methyl-3,4-tetramethylenepyrazoline (VI). Into a flask with a reflux condenser were placed 30 g of 1-dimethylaminomethylcyclohexanone-2, 25 g of methylhydrazine sulfate, 33 g of potassium carbonate and 150 ml of water. When the evolution of carbon dioxide had ceased, the mixture was boiled for 4.5 hours. The reaction mass was extracted with ether and the ether extracts dried with magnesium sulfate and vacuum distilled. We obtained 14.2 g (64%) of pyrazoline.

B.p. 92-94° (20 mm), $n^{20}D$ 1.4930, d^{20}_4 0.9714, MR_D 41.32; calc. 41.03.
Found %: C 69.12, 69.41; H 10.13, 10.18. $C_8H_{14}N_2$. Calculated %: C 69.58; H 10.14.

1-Benzyl-3,4-tetramethylenepyrazoline (VII) was synthesized similarly to the previous compound. From 19 g of benzylhydrazine we obtained 10.5 g (49%) of product.

B.p. 149-151° (4.5 mm), $n^{20}D$ 1.5595, d^{20}_4 1.0410, MR_D 66.17; calc. 66.01.
Found %: N 13.15, 13.3. $C_{14}H_{18}N_2$. Calculated %: N 13.07.

1-Phenyl-3,4-tetramethylenepyrazoline (VIII). A mixture of 50 ml of alcohol, 20 g of 1-dimethylaminomethylcyclohexanone-2 and 14 g of phenylhydrazine was boiled for 60 hours in a flask with a reflux condenser. Benzene (50 ml) was added and the solvent removed in vacuum. Vacuum distillation of the residue yielded 5.4 g (21%) of 1-phenyl-3,4-tetramethylenepyrazoline with b.p. 176-180° (9 mm) as a very thick, yellowish oil.

Found %: N 14.07, 14.13. $C_{13}H_{16}N_2$. Calculated %: N 13.98.

3-Methyl-4,5-tetramethylenepyrazoline (III). A mixture of 50 g of unpurified 2-chloroacetylcyclohexane (see above), 30 g of hydrazine hydrate and 50 ml of butanol was boiled for 10 hours. The whole reaction mixture was vacuum distilled. We obtained 32.1 g (75%, calculated on pure 2-chloroacetylcyclohexane) of pyrazoline (III).

B.p. 107-108° (9 mm), $n^{20}D$ 1.5045, d^{20}_4 1.0040, MR_D 40.78; calc. 40.62.
Found %: N 20.41, 20.46. $C_8H_{14}N_2$. Calculated %: N 20.27.

The picrolonate had m.p. 208-209° (from alcohol, in a sealed capillary).

Found %: C 54.02, 54.04; H 5.84, 5.91. $C_8H_{14}N_2 \cdot C_{10}H_8N_4O_5$. Calculated %: C 53.74; H 5.52.

4,5,6,7-Tetrahydroindazole (I). A mixture of 31 g of 3,4-tetramethylenepyrazoline and 8 g of sulfur was heated in a 70 ml Claisen flask on a metal bath (230-250°) until the evolution of hydrogen sulfide ceased (2-3 hours) and the reaction mass vacuum distilled. We obtained 17.4 g (56%) of tetrahydroindazole with b.p. 148-154° (12 mm) and m.p. 82-83° (from ligroine). The picrate had m.p. 154-155° (from alcohol).

Literature data [5]: b.p. 151° (14 mm), m.p. 84°; picrate, m.p. 155-156°.

2-Methyl-4,5,6,7-tetrahydroindazole was synthesized similarly to (I). From 13.8 g of pyrazoline (VI) we obtained 9.6 g (70%) of product.

B.p. 119-122° (30 mm), $n^{20}D$ 1.5100, d^{20}_4 1.0046, MR_D 40.50; calc. 40.89.

The picrate had m.p. 168° (from alcohol).

Literature data: b.p. 103° (13 mm); picrate, m.p. 167° [6].

2-Benzyl-4,5,6,7-tetrahydroindazole was synthesized similarly to tetrahydroindazole (I). From 10.7 g of pyrazoline we obtained 4 g (38%) of product.

B.p. 159-162° (5 mm), $n^{20}D$ 1.5720.

The picrate had m.p. 132° (from alcohol).

Literature data: b.p. 177° (10 mm); picrate, m.p. 132-133° [7].

2-Phenyl-4,5,6,7-tetrahydroindazole was synthesized similarly to tetrahydroindazole (I). From 7 g of pyrazoline (VIII) we obtained 2.7 g (39%) of tetrahydroindazole with b.p. 182-184° (9 mm) and m.p. 47-48.5° (from ligroine).

Found %: C 53.02, 52.98; H 4.27, 4.00. $C_{13}H_{14}N_2$. Calculated %: C 53.38; H 4.29.

The picrate had m.p. 125-126° (from alcohol).

Literature data: m.p. 49°; picrate, m.p. 126-127° [6].

3-Methyl-4,5,6,7-tetrahydroindazole was obtained analogously to tetrahydroindazole (I). From 13.8 g of pyrazoline (III) we obtained 5.8 g (42%) of product with b.p. 155-156° (8 mm) and m.p. 72° (from ligroine).

Found %: C 70.81, 70.70; H 8.96, 8.93. $C_8H_{12}N_2$. Calculated %: C 70.55; H 8.88.

The picrate had m.p. 213-214° (from alcohol).

Found %: N 18.81, 18.75. $C_8H_{12}N_2 \cdot C_6H_3O_7N_3$. Calculated %: N 19.18.

Indazole (II). A mixture of 7 g of tetrahydroindazole (I) with 3.6 g of sulfur was heated in a 20 ml Claisen flask on a metal bath (250-270°) until the evolution of hydrogen sulfide ceased (3-4 hours). Vacuum distillation of the reaction mixture yielded 2.1 g (35%) of indazole with b.p. 140-145° (14 mm), m.p. 148° (from ligroine).

The picrate had m.p. 138° (from alcohol).

Literature data: m.p. 148°; picrate, m.p. 137° [8].

2-Methylindazole was obtained analogously to indazole (II) in 26% yield. The b.p. 134-136° (18 mm) and the m.p. 54° (from ligroine).

Found %: C 72.72, 72.57; H 6.30, 6.21. $C_8H_8N_2$. Calculated %: C 72.73; H 6.11.

The picrate had m.p. 167° (from alcohol).

Found %: C 46.44, 46.41; H 3.24, 3.22. $C_8H_8N_2 \cdot C_6H_3N_3O_7$. Calculated %: C 46.30; H 3.03.

Literature data: m.p. 56°; picrate, m.p. 168° [9].

2-Phenylindazole was obtained similarly to indazole (II) in 26% yield. The b.p. was 178-182° (6 mm) and the m.p. 82-83° (from ligroine).

The picrate had m.p. 93° (from alcohol).

Literature data: m.p. 83-84°; picrate, m.p. 93-94° [10].

3-Methylindazole was obtained analogously to indazole (II) in 34% yield. The b.p. was 169-174° (9 mm) and the m.p. 112-113° (from ligroine).

The picrate had m.p. 198° (from alcohol).

Literature data: m.p. 113°; picrate, m.p. 199° [8].

SUMMARY

1. It was shown that dehydrogenation of 3,4- or 4,5-tetramethylenepyrazolines with sulfur led to the corresponding 4,5,6,7-tetrahydroindazoles, which could then be dehydrogenated to indazoles.

2. With methyl or phenyl radicals in position 2, dehydrogenation of the tetrahydroindazole was hindered, but the corresponding 2-substituted indazole was still formed. A benzyl group in this position led to complications.

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INTRODUCTION OF SUBSTITUENTS INTO THE BENZENE NUCLEUS OF INDOLE

IV. PREPARATION OF BROMO-, NITRO- AND AMINOINDOLES AND INDOLINES [22]

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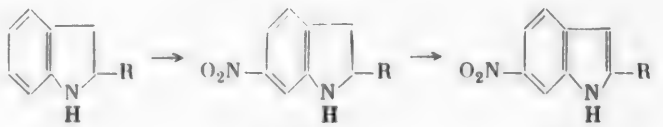
In previous communications a description was given of the preparation of indoles, substituted in the benzene nucleus, by dehydrogenation of the corresponding indolines. In connection with the fact that certain nitro and amino derivatives of indole are antimetabolites of serotonin, it seemed interesting to use the method we developed for synthesizing a series of 5- and 6-nitro- and aminoindoles and also 5-bromoindoles. We previously prepared 6-nitro-1-methylindole [1] by the following method. 1-Methylindole was reduced to 1-methylindoline. On nitration, the latter gave 6-nitro-1-methylindoline, whose dehydrogenation led to 6-nitro-1-methylindole. The same scheme was used in the present work for preparing 6-nitroindole and 6-nitro-2-methylindole.

The starting materials in the synthesis of these indole derivatives were indoline (I) and 2-methylindoline (II). Indole may be converted into indoline (I) by hydrogenation in the autoclave over Raney nickel at 100° and 100-150 atm [2]. 2-Methylindoline (II) is formed by reduction of 2-methylindole with zinc in hydrochloric acid [3].

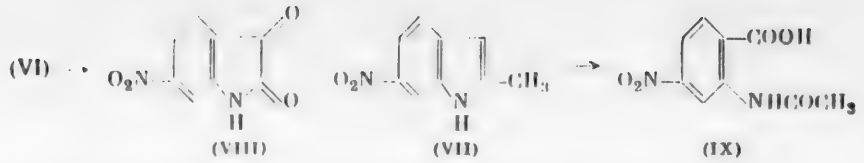


(I) R = H, (II) R = CH_3, (III) R = H, (IV) R = CH_3, (VI) R = H, (VII) R = CH_3.

The nitration of 2-methylindoline (II) with a nitrating mixture in concentrated sulfuric acid had been described in the literature [4]. Under the same conditions, indoline (I) gave a quantitative yield of 6-nitroindoline (III) on nitration. Acylation of (III) gave 1-acetyl-6-nitroindoline (V). In the present work, chloranil was used for dehydrogenation of N-substituted 6-nitroindolines. Dehydrogenation of (III) with chloranil in boiling xylene gave 6-nitroindole (VI) and dehydrogenation of (IV) gave 6-nitro-2-methylindole (VII).

6-Nitroindole was previously obtained [5] by nitration of 3-indolylcarboxylic ester and subsequent hydrolysis and decarboxylation of the 6-nitro-3-indolylcarboxylic ester formed.

Oxidation of 6-nitroindole (VI) with chromic acid in acetic acid yielded 6-nitroisatin (VIII). Oxidation of 6-nitro-2-methylindole (VII) under the same conditions gave 4-nitro-2-acetaminobenzoic acid (IX). We also obtained 4-nitroacetaminobenzoic acid by oxidation of 4-nitroacetaminotoluene [7]. A mixed melting point of the two samples was not depressed.

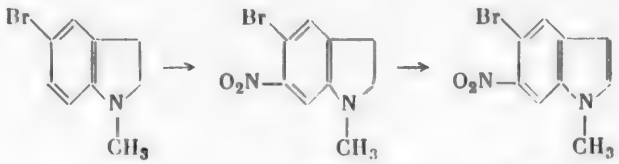


(VIII) (VII) (IX)

6-Nitroisatin was described by Giovannini and Portman [6]. The constants reported in the literature for this substance agree with those we found.

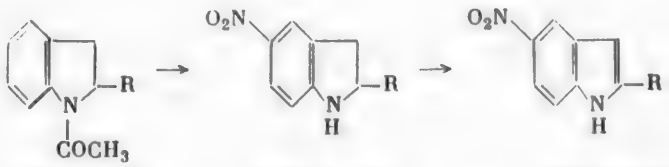
Thus, we rigidly proved that the nitro group entered position 6 in the nitration of indolines with a nitrating mixture in sulfuric acid.

The method proposed for the synthesis of indoles substituted in the benzene nucleus is convenient for the preparation of indoles containing somewhat different substituents in the benzene nucleus. Thus, by nitration of 5-bromo-1-methylindoline [8] with a nitrating mixture, we obtained a mononitro derivative, which was apparently 5-bromo-6-nitro-1-methylindoline (X). Dehydrogenation of the latter with chloranil gave 5-bromo-6-nitro-1-methylindole (XI).



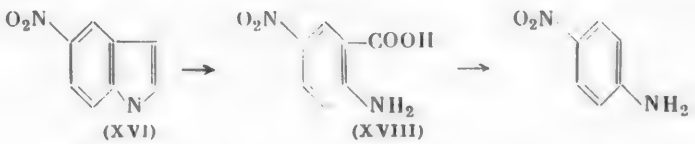
(X) (XI)

Nitration of aceto-o-toluidide formed a mixture of 3- and 5-nitro-2-acetaminotoluenes [9]. It might be expected that the nitration of 1-acetylindoline (XII) would also yield a mixture of 5- and 7-nitro-1-acetylindolines. However, it was found that the nitration of (XII) in acetic anhydride with excess concentrated nitric acid formed the 5-nitro derivative predominantly.



(XII) R = H, (XIII) R = CH_3, (XIV) R = H, (XV) R = CH_3, (XVI) R = H, (XVII) R = CH_3.

Hydrolysis yielded 5-nitroindoline (XIV) and 7-nitroindoline could not be isolated.* 5-Nitro-2-methylindoline (XV) was obtained by nitration of 2-methylindoline in acetic anhydride. Dehydrogenation of (XIV) and (XV) with chloranil in boiling xylene gave 5-nitroindole (XVI) and 5-nitro-2-methylindole (XVII) respectively. The position of the nitro group in (XVI) was demonstrated by the fact that oxidation of it with chromic acid yielded 5-nitro-2-aminobenzoic acid (XVIII), whose decarboxylation by boiling with 50% sulfuric acid gave p-nitroaniline.



(XVI) (XVIII)

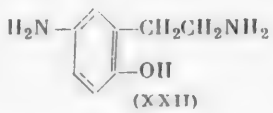
*A small amount of a dinitro derivative was obtained, which was apparently 5,7-dinitroindoline.

5-Nitroindoline was obtained previously [10] by nitration of 1-acetylindoline with a nitrating mixture in concentrated sulfuric acid, but the structure of the nitroindoline obtained was not demonstrated strictly at that time. 5-Nitro-2-methylindoline was synthesized previously by nitration and subsequent hydrolysis of 1-nitroso-2-methylindoline [11]; the position of the nitro group was not demonstrated. The constants presented in the literature agree with those we found.

By direct nitration of 2-methylindole, Walter and Clemen were able to isolate a mononitro derivative with m.p. 170° [12]. The melting point of 5-nitro-2-methylindole we obtained was 171.5-172.5°. Apparently the nitro group in the nitro-2-methylindole of Walter and Clemen occupied position 5.

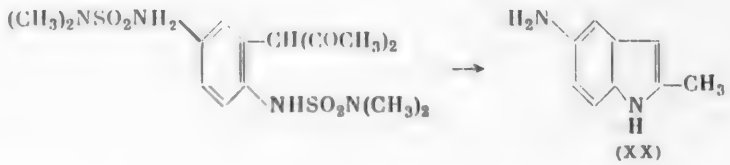
At the present time, the best method of preparing aminoindoles is the reduction of the corresponding nitroindoles with hydrazine hydrate in the presence of Raney nickel. By this method, 6-aminoindole was obtained from 6-nitroindole [13]. Using this method, we synthesized 5-aminoindole (XIX), 5-amino-2-methylindole (XX) and 6-amino-2-methylindole (XXI).

The aminoindoles were white crystalline substances, which darkened when stored in air. 5-Aminoindoles were more stable than 6-aminoindoles. 5-Aminoindole (a few milligrams in amount) was obtained previously [14] by oxidation of the p-aminophenol derivative (XXII), but this method can hardly be called preparative.



(XXII)

6-Amino-2-methylindole (XXI) was synthesized [15] (in very low yield) by hydrolysis and subsequent decarboxylation of 6-amino-2-methyl-3-carbethoxyindole. 5-Amino-2-methylindole (XX) was obtained previously [21] by the action of hydrobromic acid on the adduct of p-quinone-bis(dimethylsulfaminide) and acetylacetone.



(XX)

We used reduction with hydrazine hydrate in the presence of Raney nickel for synthesizing aminoindolines, starting from the corresponding nitroindolines. By this method we obtained 6-aminoindoline (XXIII), 6-amino-2-methylindoline (XXIV),* 6-amino-1-acetylindoline (XXV), 5-aminoindoline (XXVI) and 5-amino-2-methylindoline (XXVII).**

The aminoindolines were white crystalline substances. 6-Aminoindolines decomposed very rapidly when stored in air; they were even less stable than 6-aminoindoles. In their properties, 6-aminoindolines were very similar to m-phenylenediamine.

Only a few derivatives of indole, containing a bromine atom in the benzene nucleus, have been described. Thus, 5-bromoindole was obtained [17] by the Reissert reaction by a multistage route in very low yield. 5-Bromo-2-methylindole was synthesized starting from acetone p-bromophenylhydrazone [18]. In one of our previous communications [8], we proposed a new method of synthesizing 5-bromo-1-methylindole (by bromination of 1-methylindoline and subsequent dehydrogenation of the 5-bromo-1-methylindoline obtained).

In the present article we describe the preparation of 5-bromoindole (XXVIII) and 5-bromo-2-methylindole (XXIX) by the same method.

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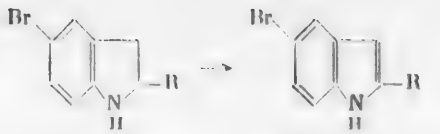
*This was described in the literature [20], but it could not be isolated previously in a pure form.

**This was obtained previously by the reduction of 5-p-phenylsulfonyl-azo-2-methylindoline or 5-nitroso-2-methylindoline with stannous chloride [16].



(XXX) R = H, (XXXI) R = CH$_3$, (XXVIII) R = H, (XXIX) R = CH$_3$.

Bromination of indoline (I) in glacial acetic acid in the presence of concentrated sulfuric acid gave 5-bromoindoline (XXX) and bromination of 2-methylindoline (II) under the same conditions gave 5-bromo-2-methylindoline (XXXI). 5-Bromo-1-acetylindoline, obtained by acetylating 5-bromoindoline with acetic anhydride, had the same properties as the 5-bromo-1-acetylindoline described in the literature [10], which was obtained by bromination of 1-acetylindoline. Consequently, in the bromination of both indoline and 1-acetylindoline the bromine entered position 5 of the indole ring.

Dehydrogenation of (XXX) with chloranil in boiling xylene gave 5-bromoindole (XXVIII) and dehydrogenation of (XXXI) gave 5-bromo-2-methylindole (XXIX). The properties of the 5-bromoindoles we obtained corresponded with those described in the literature. Starting from (XXIX), we synthesized 5-bromo-2-methylgramine, whose properties also agreed with those described in the literature.

EXPERIMENTAL

6-Nitroindoline (III). With stirring and cooling below +5°, 11.9 g of indoline (I) was added dropwise to 100 ml of concentrated sulfuric acid; with vigorous stirring and cooling below 0°, a mixture of 4.4 ml of HNO_3 (d 1.5) and 100 ml of concentrated H_2SO_4 was added dropwise to the solution obtained. One hour after the end of the addition of the nitrating mixture, the reaction mixture was poured onto ice and neutralized with sodium carbonate solution. We obtained 16 g (quantitative yield) of orange crystals of 6-nitroindoline. The m.p. was 66.5-67.5° (from heptane).

Found: N 16.98. $C_8H_8O_2N_2$. Calculated %: N 17.06.

1-Acetyl-6-nitroindoline (V) was obtained by boiling 6-nitroindoline (III) with acetic anhydride. The yellow crystals had m.p. 154.5-155° (from aqueous alcohol).

Found %: N (not considering the nitrogen of the nitro group) 6.90. $C_{10}H_{10}O_3N_2$. Calculated %: N (indoline) 6.80.

6-Nitroindole (VI). A solution of 6.1 g of 6-nitroindoline and 9.1 g of chloranil in xylene (300 ml) was boiled for 5 hours, cooled, shaken several times with a 20% solution of alkali and filtered and the xylene solution washed successively with water, hydrochloric acid (1 : 1) and water. Removal of the solvent yielded 5 g (82%) of 6-nitroindole. The product was a yellow, crystalline substance. The m.p. was 141-142° (from benzene and then from aqueous alcohol). According to data in [5]: m.p. 139-140.5°.

Found %: C 59.28; H 3.91. $C_8H_6O_2N_2$. Calculated %: C 59.24; H 3.73.

6-Nitro-2-methylindole (VII). A solution of 5.6 g of 6-nitro-2-methylindoline (IV) [4] and 7.7 g of chloranil in 200 ml of xylene was boiled for 7 hours. After appropriate treatment, the xylene was removed to yield 4.25 g (81%) of 6-nitro-2-methylindole. The m.p. was 113.5-114.5° (from ligroine).

Found %: C 60.92; H 4.85; N 15.96. $C_9H_8O_2N_2$. Calculated %: C 61.36; H 4.58; N 15.90.

6-Nitroisatin (VIII). A solution of 1.5 g of CrO_3 in 10 ml of water was added dropwise to a solution of 1.3 g of 6-nitroindole (VI) in 100 ml of acetic acid. The reaction mixture was heated on a boiling water bath for half an hour, then poured into water, filtered and extracted several times with ether and then with chloroform. Evaporation of the ether and chloroform yielded orange crystals of 6-nitroisatin, suspended in acetic acid. The yield was 0.7 g (45%). The m.p. was 300° (decomp.) (from aqueous acetic acid). The product sublimed on heating. According to data in [6]: m.p. 288-290° (decomp.).

Found %: N 14.12. $C_8H_4O_4N_2$. Calculated %: N 14.58.

The phenylhydrazone of 6-nitroisatin was prepared in dilute acetic acid. The red platelets had m.p. 265-266° (decomp.) (from dilute acetic acid).

Found %: N 19.58. $C_{14}H_{10}O_3N_4$. Calculated %: N 19.85.

Oxidation of 6-nitro-2-methylindole (VII). With stirring, a solution of 1.24 g of CrO_3 in 5 ml of water was added dropwise to a solution of 1.07 g of (VII) in 30 ml of acetic acid. The reaction mixture gave off heat. The solution was heated for 1 hour on a boiling water bath and then poured into water, hydrochloric acid added and the reaction product extracted with chloroform. The solvent was removed and the residual substance recrystallized from water. We obtained 0.48 g (33%) of 4-nitro-2-acetaminobenzoic acid (IX). The m.p. was 225-226°. The melting point of 4-nitro-2-acetaminobenzoic acid, obtained by oxidation of 4-nitro-2-acetaminotoluene with $KMnO_4$ [7], was 223-225°. According to data in [7]: m.p. 220-222°. A mixed melting point of the two samples was not depressed.

6-Nitro-5-bromo-1-methylindoline (X). 6.9 g of 5-bromo-1-methylindoline [8] was dissolved with stirring and cooling below 0°, in 50 ml of concentrated sulfuric acid and a mixture of 1.5 ml of HNO_3 (d 1.5) and 10 ml of concentrated H_2SO_4 added with stirring and cooling (below 0°). After 1 hour, the reaction mixture was poured onto ice and neutralized with sodium carbonate solution. We obtained 7.8 g (quantitative yield) of dark red crystals. For analysis, the substance was recrystallized from octane and then from aqueous alcohol. The orange crystals had m.p. 73-74°.

Found %: C 42.01; H 3.34; $C_9H_9O_2N_2Br$. Calculated %: C 42.04; H 3.53.

6-Nitro-5-bromo-1-methylindoline (XI). A solution of 3 g of 6-nitro-5-bromo-1-methylindoline (X) and 2.85 g of chloranil in xylene was boiled for a few hours. The reaction mixture was treated as in the preparation of 6-nitroindole. Removal of the xylene in vacuum yielded 1.6 g (54%) of a yellow crystalline substance. M.p. 167-168° (from benzene and then from alcohol).

Found %: C 42.13; H 2.90. $C_9H_7O_2N_2Br$. Calculated %: C 42.37; H 2.77.

5-Nitroindoline (XIV). 11.9 g of indoline was dissolved in 150 ml of acetic anhydride and 8.5 ml of concentrated HNO_3 (d 1.5) was added dropwise with stirring. The temperature was kept within the range 10-12°. After the addition of the HNO_3, the reaction mixture was poured into water and the precipitate of the solid acetyl derivative of 5-nitroindoline collected. To the substance obtained was added 100 ml of concentrated hydrochloric acid and the mixture boiled for 30 minutes. The solution was filtered. The dark tarry substance remaining on the filter was boiled with water and recrystallized from xylene and then acetic acid to give 1 g of dinitroindoline. The product formed yellow crystals (after a xylene solution of the substance had been boiled with charcoal). The m.p. was 243-244° (from alcohol).

Found %: C 45.90; H 3.32; N 20.12. $C_8H_7O_4N_3$. Calculated %: C 45.93; H 3.38; N 20.09.

The mother solution was carefully neutralized with sodium bicarbonate solution. After the addition of the first portions of sodium bicarbonate, a black tar precipitated and this was best removed. Subsequent addition of soda precipitated 11.8 g (74%) of a yellow precipitate of 5-nitroindoline (XIV). The m.p. was 86-88°. For analysis, the substance was recrystallized from heptane and then several times from water. The m.p. was 91-91.5°. According to data in [10]: m.p. 92-93°.

Found %: C 58.53; H 4.98; N 16.82. $C_8H_8O_2N_2$. Calculated %: C 58.52; H 4.92; N 17.06.

5-Nitro-2-methylindoline (XV). A solution of 6.65 g of 2-methylindoline in 5 ml of acetic anhydride was boiled for 1 hour and then with stirring and cooling below 10°, 8.2 ml of HNO_3 (d 1.35) was added to the reaction mixture dropwise over a period of 2 hours. The brown solution was poured onto ice. 5-Nitro-2-methyl-1-acetylindoline precipitated as an oil, which crystallized on standing.* It was collected and boiled with concentrated hydrochloric acid (100 ml) for 1 hour. The reaction mixture was poured into water and neutralized with sodium bicarbonate. The precipitated oil crystallized rapidly. For purification, the substance was again dissolved in dilute hydrochloric acid and precipitated with sodium bicarbonate. The yield of 5-nitro-2-methylindoline was 6.9 g (63%). The m.p. was 72-73°. For analysis, the substance was recrystallized from heptane. The m.p. was 78-79°. According to data in [11]: m.p. 82°.

Found %: C 59.92; H 6.00; N 16.01. $C_9H_{10}O_2N_2$. Calculated %: C 60.66; H 5.65; N 15.73.

*If nitric acid (d 1.5) was used for nitration of the 2-methyl-1-acetylindoline, then the 5-nitro-2-methyl-1-acetylindoline could not be isolated in a crystalline form.

5-Nitroindole (XVI). A solution of 7.9 g of 5-nitroindoline (XIV) and 11.7 g of chloranil in xylene was boiled for 10 hours. The reaction mixture was then treated as in the preparation of 6-nitroindole. Removal of the xylene yielded 5.4 g (68%) of 5-nitroindole with m.p. 133-135°. For analysis, the substance was recrystallized from benzene and then from octane. The m.p. was 135-137°. A mixture with 6-nitroindole gave a depressed melting point. The bright yellow crystals were soluble in hot water.

Found %: C 58.97; H 3.73; N 17.18. $C_8H_6O_2N_2$. Calculated %: C 59.24; H 3.73; N 17.28.

5-Nitro-2-methylindole (XVII). A solution of 11.7 g of 5-nitro-2-methylindoline (XV) and 16.2 g of chloranil in xylene was boiled for 5 hours and then treated as usual. After removal of the xylene, we obtained 7.45 g (65%) of 5-nitro-2-methylindole. The m.p. was 171.5-172.5° (from heptane).

Found %: C 60.82; H 4.63. $C_9H_8O_2N_2$. Calculated %: C 61.36; H 4.58.

Oxidation of 5-nitroindole (XVI) to 5-nitro-2-aminobenzoic acid (XVIII). 1 g of (XVI) was dissolved in acetic acid (100 ml), the solution heated on a boiling water bath and a solution of 1.2 g of chromium trioxide in 10 ml of water added dropwise. The reaction mixture was heated for 1 hour on a boiling water bath, poured into water, filtered and extracted with ether in an extractor. The ether extract, which contained a considerable amount of acetic acid, was evaporated to a volume of 10 ml to give a suspension of 5-nitro-2-aminobenzoic acid (XVIII) in acetic acid. (XVIII) was collected. We obtained 1 g of light brown crystals, which decomposed when heated to 250°. The substance was recrystallized from aqueous alcohol with charcoal and then several times from water. The m.p. was 275.5-276° (decomp.). The substance formed yellow needles. According to data in [19]: m.p. 263°.

Found %: N 15.30. $C_7H_6O_4N_2$. Calculated %: N 15.38.

A few tenths of a gram of substance (XVIII) was boiled with 50% sulfuric acid for 1 hour. The solution obtained was filtered, neutralized with sodium bicarbonate and extracted with ether. Evaporation of the solvent yielded a small amount of yellow crystals with m.p. 140-144°. After recrystallization from water, the substance had m.p. 145-146°. A mixed melting point with p-nitroaniline was not depressed.

5-Aminoindole (XIX). To a solution of 5.4 g of 5-nitroindole (XVI) in 50 ml of alcohol was added a small amount of Raney nickel and over a period of a few hours, 100 ml of hydrazine hydrate was introduced dropwise into the boiling reaction mixture. The solution was filtered, the alcohol removed in vacuum and the 5-aminoindole distilled. The b.p. was ≈190° (6 mm). The white crystalline substance sublimed readily. We obtained 3.6 g (82%) of product with m.p. 123-124°. After recrystallization from heptane, the product had m.p. 129-130° decomp.). The substance decomposed very rapidly when heated and when in light. For determining the melting point, a sealedcapillary was introduced into the apparatus, heated to 80°. According to data in [14]: m.p. 127-129°.

Found %: C 72.77; H 6.35. $C_8H_8N_2$. Calculated %: C 72.68; H 6.10.

The benzoyl derivative was prepared by dissolving the aminoindole in benzene and shaking the solution with 20% alkali and excess benzoyl chloride. The reaction mixture was left overnight; on standing, the benzene layer deposited a precipitate. Evaporation of the benzene solution yielded some more of the substance. The product was recrystallized from benzene with charcoal and then several times from benzene. The m.p. was 166-167°.

Found %: N 11.69. $C_{15}H_{12}ON_2$. Calculated %: N 11.85.

5-Amino-2-methylindole (XX). 6 g of 5-nitro-2-methylindole (XVII) was dissolved in 200 ml of alcohol and reduced with hydrazine hydrate in the presence of Raney nickel. The reduction lasted for 2 days. Removal of the solvent in vacuum yielded a dark, crystalline substance. The yield was 3.8 g (76%). The m.p. was 156-156.5° (from water and then from heptane). According to data in [21]: m.p. 157-159°.

Found %: C 73.55; H 7.17. $C_9H_{10}N_2$. Calculated %: C 73.93; H 6.89.

5-Benzoylamino-2-methylindole was obtained by benzoylation of 5-amino-2-methylindole by the Schotten-Baumann method. The m.p. was 192-192.5° (from benzene).

Found %: N 11.50. $C_{16}H_{14}ON_2$. Calculated %: N 11.19.

6-Amino-2-methylindole (XXI). 7 g of 6-nitro-2-methylindole (VII) was reduced as described for the preparation of 5-aminoindole (XIX). The solvent was removed and the reaction product vacuum distilled. After two

distillations, the 6-amino-2-methylindole had m.p. 170-177° (4 mm). The yield was 2.5 g (43%). The substance darkened very rapidly in air. It crystallized on standing. The m.p. was 84-85° (from carbon tetrachloride). According to data in [15]: m.p. 82°.

Found %: N 18.72. $C_9H_{10}N_2$. Calculated %: N 19.16.

6-Benzoylamino-2-methylindole was obtained by benzoylating 6-amino-2-methylindole by the Schotten-Baumann method. The m.p. was 210° (from aqueous alcohol). According to data in [15]: m.p. 209°.

6-Aminoindoline (XXIII). To a solution of 16.2 g of 6-nitroindoline (III) in 100 ml of methyl alcohol was added 0.5 g of Raney nickel and 100 ml of hydrazine hydrate introduced in small portions. The temperature of the reaction mixture was kept at 50-60°. After a few hours the solution became colorless. The catalyst was filtered from the solution and the methyl alcohol removed in vacuum. Vacuum distillation of 6-aminoindoline was very difficult as the substance foamed strongly. The b.p. was 138°, (1 mm). The turbid, yellow liquid rapidly darkened in air and crystallized rapidly on cooling. The m.p. was 67-68°. We obtained 10.3 g (77%) of product.

Found %: N 20.85. $C_8H_{10}N_2$. Calculated %: N 20.88.

Boiling (XXIII) with acetic anhydride yielded 6-acetamino-1-acetylindoline. The m.p. was 269-271° (from 20% acetic acid).

Found %: C 66.16; H 6.49. $C_{12}H_{14}O_2N_2$. Calculated %: C 66.02; H 6.46.

6-Amino-1-acetylindoline (XXV). 3.80 g of 6-nitro-1-acetylindoline (V), 20 ml of concentrated hydrochloric acid and 30 g of stannous chloride were heated for 25 minutes on a water bath, poured into water and made strongly alkaline with KOH. The substance obtained was collected and washed with water on a filter. We obtained 2.9 g (89%) of a dark, crystalline substance. Recrystallization from alcohol with charcoal yielded colorless crystals with m.p. 179-179.5°. The product was very sparingly soluble in the usual organic solvents (ether, benzene and chloroform).

Found %: N 15.95. $C_{10}H_{12}ON_2$. Calculated %: N 15.20.

Acetylation of (XXV) with acetic anhydride gave 6-acetamino-1-acetylindoline, identical with the acetylation product of 6-aminoindoline.

6-Amino-2-methylindoline (XXIV). 3.7 g of 6-nitro-2-methylindoline (IV) was reduced with hydrazine hydrate under the same conditions as for 6-nitroindoline. The boiling point of (XXIV) was 175-180° (17 mm). According to data in [7]: m.p. 182-184°. We obtained 2.8 g (91%) of product. The yellow, viscous substance darkened very rapidly in air. Recrystallization from heptane or ether yielded white crystals with m.p. 61-62°.

Found %: N 18.68. $C_9H_{12}N_2$. Calculated %: N 18.90.

The hydrochloride was obtained by passing dry hydrogen chloride into a solution of (XXIV) in ether. The m.p. was 230-235° (decomp.). The substance was hygroscopic. According to data in [20]: m.p. 235-238°.

5-Aminoindoline (XXVI) was obtained by reducing 5-nitroindoline (XIV) under the same conditions as described for the preparation of 6-aminoindoline. After removal of the solvent, the substance crystallized. From 5 g of (XIV) we obtained 4 g (97%) of 5-aminoindoline (XXVI) as a white crystalline substance with m.p. 67-68.5° (from heptane).

Found %: N 20.99. $C_8H_{10}N_2$. Calculated %: N 20.88.

For preparation of the diacetyl derivative, substance (XXVI) was boiled in acetic anhydride and the acetic anhydride removed in vacuum; the 5-acetamino-1-acetylindoline melted at 211-212.5° (from water).

Found %: N 12.80. $C_{12}H_{14}O_2N_2$. Calculated %: N 12.83.

5-Amino-2-methylindoline (XXVII). This substance was obtained by reduction of (XV) in 93% yield. The b.p. was 155-158° (9 mm). The m.p. was 92° (from heptane). According to data in [16]: m.p. 93.5°.

Found %: N 19.00. $C_9H_{12}N_2$. Calculated %: N 18.90.

5-Bromo-2-methylindoline (XXXI). 13.3 g of 2-methylindoline was dissolved in 35 ml of glacial acetic acid; 5.2 ml of conc. H_2SO_4 was added and then 16 g of bromine was introduced dropwise with stirring. After

addition of the bromine, the reaction mixture was stirred for a further 1 hour and then poured into a 20% solution of alkali. The bromoindoline was steam distilled and extracted from the distillate with ether. The ether extract was dried over potassium carbonate, the ether removed and the residue vacuum distilled. A fraction with b.p. 110-140° (3 mm) was collected. The yield was 13.4 g (63.5%). Redistillation gave a fraction with b.p. 130-145° (3 mm), 10.54 g (49.5%). The substance distilled with partial decomposition. The substance was redistilled for analysis. The b.p. was 132-133.5° (3 mm). The thick, almost colorless liquid rapidly darkened in air.

d^{20}_4 1.4550, $n^{20}D$ 1.6085, MR_D 50.34. $C_9H_{10}NBrF_3$.* Calculated 50.42.
Found %: C 50.71; H 4.50. $C_9H_{10}NBr$. Calculated %: C 50.97; H 4.75.

Benzoylation by the Schotten-Baumann method yielded 5-bromo-2-methyl-1-benzoylindoline. The m.p. was 157° (from alcohol).

Found %: C 60.89; H 4.54. $C_{16}H_{14}ONBr$. Calculated %: C 60.73; H 4.47.

5-Bromoindoline (XXX). 23.8 g of indoline was dissolved with cooling in 60 ml of glacial acetic acid, 10.4 ml of H_2SO_4 added and 32 g of bromine introduced dropwise with stirring. After the addition of the bromine, stirring was continued for a further 3 hours. The reaction mixture was poured into 40% alkali and then treated as in the case of 5-bromo-2-methylindoline. On distillation, a fraction with b.p. 107-135° (2 mm) was collected. The yield was 28.8 g (72.7%). Redistillation yielded a substance with b.p. 114-114.5° (2 mm). The thick, colorless liquid rapidly darkened in air. It distilled with decomposition.

d^{20}_4 1.5240, $n^{20}d$ 1.6311, MR_D 46.30. $C_8H_8NBrF_3$. Calculated 46.10.
Found %: N 7.02. C_8H_8NBr. Calculated %: N 7.07.

5-Bromo-1-acetylindoline was obtained by boiling 5-bromoindoline with acetic anhydride with subsequent dilution of the reaction mixture with water. The m.p. was 119-119.5° (from alcohol). According to data in [10]: m.p. 118-119°.

Found %: N 5.93. $C_{10}H_{10}ONBr$. Calculated %: N 5.84.

5-Bromo-2-methylindole (XXIX). A solution of 4.5 g of 5-bromo-2-methylindoline (XXXI) and 5.2 g of chloranil in xylene was boiled for 30 minutes and treated as described for the preparation of 6-nitroindole. The xylene was removed in vacuum and the residue distilled. The b.p. was 155-162° (4 mm). The substance distilled with partial decomposition. The yield was 2.4 g (54%). The white crystals had m.p. 97-98° (from heptane). They became red when stored in air. According to data in [14]: m.p. 93-96°.

Found %: N 6.80. C_9H_8NBr. Calculated %: N 6.67.

5-Bromo-2-methylskatyldimethylamine (5 bromo-2-methylgramine) was obtained by reacting a solution of 5-bromo-2-methylindole in acetic acid with formalin and an aqueous solution of dimethylamine. The m.p. was 145-147° (from acetone). According to data in [17]: m.p. 143-145° (from aqueous acetone).

5-Bromoindole (XXVIII). A solution of 3.5 g of 5-bromoindoline (XXX) and 4.3 g of chloranil in xylene was boiled for 1.5 hours. The reaction mixture was then treated as in the preparation of 5-bromo-2-methylindole. After removal of the xylene, the reaction product crystallized. Recrystallization from heptane yielded 1.6 g (47%) of 5-bromoindole. For analysis, the substance was sublimed in vacuum (3 mm). The flask was heated on a water bath to 70°. The colorless crystals had m.p. 92-93°. According to data in [18]: m.p. 88.5-89°.

Found %: C 48.70; H 2.96. C_8H_6NBr. Calculated %: C 49.02; H 3.09.

SUMMARY

1. It was shown that in the nitration of indolines with a nitrating mixture in concentrated sulfuric acid, the nitro group entered position 6 of the indoline ring and in nitration of 1-acetylindolines with nitric acid, position 5 of the indoline ring.

2. Dehydrogenation of appropriate nitroindolines yielded 6-nitroindole, 6-nitro-2-methylindole, 5-nitroindole and 5-nitro-2-methylindole.

*The molecular refraction increment for the nitrogen was taken as 3.59 (as for a secondary aliphatic aromatic amine).

3. Reduction of nitroindoles and nitroindolines with hydrazine hydrate in the presence of Raney nickel yielded 5-aminoindole, 5-amino-2-methylindole, 5-aminoindoline, 5-amino-2-methylindoline, 6-aminoindoline, 6-amino-2-methylindoline and 6-amino-2-methylindole.

4. A new method is proposed for the synthesis of 5-bromoindole and 5-bromo-2-methylindole by dehydrogenation of the corresponding indolines.

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INTERACTION OF DIALKYLPHOSPHOROUS ACIDS WITH ALDEHYDES AND KETONES

XXI. DI-β,β'-DICHLOROISOPROPYL ESTERS OF SUBSTITUTED α-HYDROXYMETHYLPHOSPHINIC ACID

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Continuing our work on the synthesis of various esters of α-hydroxyalkylphosphinic acids by condensation of dialkylphosphorus acids with carbonyl compounds [1], we extended the investigation to di-β,β'-dichloroisopropylphosphorous acid. We previously studied the interaction of di-tert-(1,1,1-trichloro)-butylphosphorous acid and other chlorine-substituted acids of similar structure with aldehydes and ketones [2] and found that the condensation leading to the formation of chlorine-substituted esters of α-hydroxyalkylphosphinic acids proceeded without catalyst at room temperature. Such a reaction course may be explained by the stability of the enol form of the dialkylphosphorous acids studied, which is caused by the presence of the chlorine atoms in the ester radicals of the acid. It seemed interesting to study the condensation of di-β,β'-dichloroisopropylphosphorous acid and other acids, containing chlorine atoms in ester radicals of various structures.

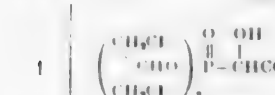
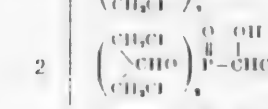
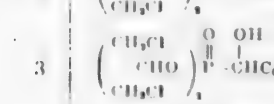
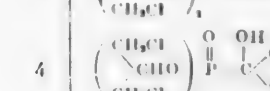
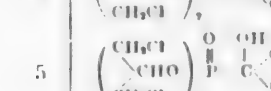
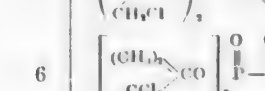
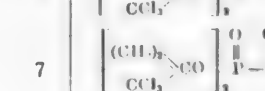
Di-β,β'-dichloroisopropylphosphorous acid was prepared by the action of water on the corresponding acid chloride.

$$\left(\begin{matrix}CH_2Cl\\ \diagdown\!\!\diagup CHO\\ CH_2Cl\end{matrix}\right)_2 PCl \rightarrow \left(\begin{matrix}CH_2Cl\\ \diagdown\!\!\diagup CHO\\ CH_2Cl\end{matrix}\right)_2 POH$$

Di-β,β'-dichloroisopropylphosphorous acid was usually condensed with aldehydes and ketones by mixing equimolecular amounts of the reaction components. The reaction proceeded without catalyst at room temperature. Many aldehydes and ketones reacted with di-β,β'-dichloroisopropylphosphorous acid, but it was best to determine and then isolate those condensation products which were obtained in the crystalline form. The appearance of the first crystals of di-β,β'-dichloroisopropyl esters was considered the beginning of the reaction and the conversion of the reaction mixture into a solid crystalline mass, the end. The esters were recrystallized from 96% alcohol. The course of the reaction with time and the physical constants of the esters obtained and their analyses are presented in the table (Nos. 1-5). In addition, the table also gives data for di-tert-(1,1,1-trichloro)-butyl esters of α-hydroxy-β-chloroisopropylphosphinic and α-hydroxy-β,β'-dichloroisopropylphosphorous acids (Nos. 6 and 7), which are published for the first time. All the esters were odorless, white, crystalline substances, which were insoluble in water, but readily soluble in organic solvents.

In addition to the fully characterized substances given, we also prepared the condensation products of di-β,β'-dichloroisopropylphosphorous acid with acetaldehyde, propionaldehyde, butyraldehyde, isovaleraldehyde, cyclopentanone etc., but these were obtained as sirupy liquids, whose purification was difficult.

Esters of Substituted α-Hydroxymethylphosphinic Acid

Sample No.	Formula of ester	Reaction time (in hr)	Time for 1st ester cryst. to appear (hr)	Melting point	Yield (in %)	Cl content* (in %) found	Cl content* (in %) calc.	P content* (in %) found	P content* (in %) calc.
1		24	0.5	110–112°	71.0	55.20	54.99	6.81	6.86
2		190	150	80.5–81.5	67.0	34.37	34.59	7.39	7.55
3		90	72	120–121	55.0	31.08	31.16	6.64	6.80
4		252	216	79–80	60.0	39.10	39.18	8.40	8.56
5		160	125	89–91	68.0	34.75	35.27	7.49	7.70
6		384	46	151	41.0	50.26	50.30	6.16	6.28
7		6**	2	176–177	74.0	53.64	53.75	5.71	5.87

*The chlorine and phosphorous contents given in the "found" column are the average of two determinations.

**The reaction was carried out at 120°.

EXPERIMENTAL

Preparation of di-β,β'-dichloroisopropylphosphorous acid. 72.1 g of the acid chloride of di-β,β'-dichloroisopropylphosphorous acid was placed in a three-necked flask, fitted with a dropping funnel, mechanical stirrer, thermometer, and gas outlet tube. The flask was cooled in snow and salt while 4.0 g of water was added dropwise at such a rate that the temperature in the flask did not exceed 0°. Removal of the hydrogen chloride in vacuum yielded 65.6 g (96.5%) of acid as a colorless liquid.

d^{20}_4 1.4917, $n^{20}D$ 1.4976, MR_D 59.51. $C_6H_{11}O_3Cl_4P$. Calculated 59.73.

Condensation of di-β,β'-dichloroisopropylphosphorous acid with aldehydes and ketones. The condensation of di-β,β'-dichloroisopropylphosphorous acid with aldehydes and ketones was carried out in ampoules, into which were placed 4 g of acid and an equimolecular amount of aldehyde or ketone. The ampoules were kept at room temperature. The course of the reaction was followed from the change in viscosity in the reaction mixture and then from the appearance of crystals and the change of the whole mixture into a crystalline mass. The crystalline chlorine-substituted esters of α-hydroxyalkylphosphinic acids were recrystallized from alcohol (rectified). The results are presented in the table.

The liquid, sirupy condensation products were subjected to various operations in order to crystallize them, but all attempts were unsuccessful.

SUMMARY

It was shown that di-β,β'-dichloroisopropylphosphorous acid reacts with aldehydes and ketones without catalyst at room temperature and gives di-β,β'-dichloroisopropyl esters of α-hydroxyalkylphosphinic acids.

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HYDROGENATION OF UNSATURATED COMPOUNDS IN THE PRESENCE OF COLLOIDAL PALLADIUM

XI. HYDROGENATION OF VINYLACETYLENE

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In a series of works in which one of us participated, a study was made of the hydrogenation of various unsaturated compounds in the presence of colloidal palladium, including the hydrogenation of vinylalkylacetylenes and alkenylacetylenes. Certain problems were elucidated connected with the order of addition of hydrogen in relation to the structure of the substance and also with the effect of different additives on the composition of the hydrogenation products. In addition, it was shown that in a series of cases, the addition of small amounts of certain organic substances increased the selective action of colloidal palladium in the sence of the predominant addition of hydrogen at the triple bond [1].

In view of the great practical value of selective hydrogenation of vinylacetylene to butadiene, we decided to study the effect of various additives on the composition of the hydrogenation products of the given hydrocarbon in the presence of colloidal palladium.

TABLE 1

Average Yield of Butadiene (in %), Calculated on the Vinylacetylene Reacting

Expt. No.	Name of additive	Ratio of vinylacetylene to hydrogen (in moles)		
		1 : 1	1 : 0.75	1 : 0.5
1	Without additive	66.3	79.5	80.6
2	p-Thiocyanochlorobenzene	66.7	83.7	—
3	Lead acetate	78.3	83.0	84.8
4	Copper acetate	74.0	78.8	—
5	Pyridine	59.0	70.7	72.4
6	Quinoline	70.5	77.9	85.3
7	Diethylamine	60.9	71.2	65.1
8	Aniline	74.1	71.2	70.8

The hydrogenation of vinylacetylene in the presence of various catalysts has been studied by many authors [2-5, 9]. It was first studied thoroughly by S. V. Lebedev and his co-workers, who used colloidal palladium together with other catalysts. An essential defect in their work, as was noted by the authors themselves, was the high gas losses (up to 44%) during their desorption from the hydrogenation apparatus. Considering this fact, we

TABLE 2

Hydrogenation in the Ratio 1:1

Additives		Amt. of vinylacetylene taken (in ml)	Amt. of hydrogen absorbed (in ml)	Hydrogenation time (in min)	Analysis of hydrogenation products				
					total amt. of unsaturated hydrocarbons		percent composition of unsaturated hydrocarbons		
Name	amt. (in % of weight of vinylacetylene)				(in ml)	(in %)	vinylacetylene	butadiene	butylenes
Without additive		360	360	78	301	83.6	21.4	61.0	17.6
The same		393	393	88	333	84.7	22.5	65.5	12.0
The same		371	371	83	328	87.1	23.4	61.1	15.5
p-Thiocyanochlorobenzene	0.046	375	375	118	311	83.0	17.1	67.4	15.5
The same	0.096	359	359	103	306	85.2	18.6	67.3	14.1
Lead acetate	0.115	373	373	175	340	91.2	26.3	67.0	6.7
The same	0.12	363	363	160	322	88.9	25.2	68.8	6.0
The same	0.115	376	376	183	333	88.6	23.4	67.9	8.7
Copper acetate	0.115	378	378	173	350	92.7	31.9	56.2	11.9
The same	0.110	391	391	172	363	92.9	31.4	56.3	12.3
Pyridine	21.7	397	397	84	325	81.7	19.6	60.5	19.9
The same	21.3	404	404	85	345	85.3	16.9	59.4	23.7
Quinoline	23.1	373	373	92	323	86.6	19.3	65.7	15.0
The same	11.1	388	388	100	338	87.0	18.5	70.2	11.3
Diethylamine	3.9	388	388	131	332	85.5	13.9	60.1	26.0
The same	4.0	380	380	135	327	86.0	12.6	66.0	21.4
Aniline	11.4	380	380	85	322	87.4	20.1	67.7	12.2

TABLE 3

Hydrogenation in the Ratio 1:0.75

Additives		Amt. of vinylacetylene taken (in ml)	Amt. of hydrogen absorbed (in ml)	Hydrogenation time (in min)	Analysis of hydrogenation products				
					total amt. of unsaturated hydrocarbons		percent composition of unsaturated hydrocarbons		
Name	amt. (in % of weight of vinylacetylene)				(in ml)	(in %)	vinylacetylene	butadiene	butylenes
Without additive		393	294	73	362	92.2	39.1	55.6	5.3
The same		394	295	67	354	89.9	40.4	55.2	4.4
p-Thiocyanochlorobenzene	0.093	373	280	76	337	90.5	42.8	56.9	0.3
The same	0.084	407	306	78	374	91.8	45.2	52.7	2.1
Lead acetate	0.12	360	281	104	322	89.6	42.7	53.9	3.4
The same	0.23	369	277	144	348	94.3	41.8	56.8	1.4
Copper additive	0.11	388	291	127	365	94.1	48.7	45.4	5.9
Pyridine	10.7	403	303	59	345	85.6	32.5	59.2	8.3
The same	20.4	422	316	60	351	83.2	30.7	64.1	5.2
The same	30.9	419	314	57	355	84.8	30.4	61.6	8.0
Quinoline	11.2	384	288	67	343	89.2	32.8	61.3	5.9
The same	21.9	393	295	83	350	88.9	32.8	62.6	4.6
Diethylamine	3.97	380	285	76	338	89.1	29.8	58.7	11.5
Aniline	11.55	373	280	49	330	88.5	23.7	63.4	12.9
The same	22.96	375	282	53	334	89.0	22.6	64.1	13.3

first developed experimental conditions which allowed us to reduce these losses considerably, especially in experiments where the molar ratio of vinylacetylene to hydrogen was less than 1:1.

The gas mixture collected after hydrogenation was analyzed quantitatively for the content of vinylacetylene, butadiene, and butylenes. The hydrogenation was carried out with ratios of vinylacetylene to hydrogen (in moles) of 1 : 1, 1 : 0.75, and 1 : 0.5. As additives we used various amounts of p-thiocyanochlorobenzene, lead and copper acetates, pyridine, quinoline, aniline, and diethylamine.

Table 1 shows that the most active additive was lead acetate, especially in hydrogenation at a ratio of 1 : 1, both in increasing the butadiene yield and decreasing the butylene content and in strongly slowing the hydrogenation process (Table 2). At other ratios, the butadiene yield increased and therefore the effect of lead acetate was less noticeable.

The next active additive both with respect to the butadiene yield and the slowing of the reaction was found to be copper acetate (Tables 1, 2 and 3). Its effect at other ratios was also less noticeable.

The effect of p-thiocyanochlorobenzene appeared mainly as a reduction in the yield of butylenes, which was also a positive factor.

The organic bases were used in considerably larger amounts than the previous additives. Some increase in the butadiene yield was observed in the presence of quinoline. Aniline had a positive effect only at ratios of 1 : 1, while at other ratios it even had a negative action. Diethylamine slowed the reaction, decreased the butadiene yield and increased the formation of butylenes. Pyridine behaved in approximately the same way with the difference that it had hardly any effect on the hydrogenation rate.

Thus, it was shown that in the hydrogenation of vinylacetylene with colloidal palladium both in the absence and presence of organic additives, butadiene was formed predominantly, but butylenes were also formed. Some of the additives used increased the selective action of the catalyst and noticeably slowed the course of the hydrogenation.

EXPERIMENTAL

The vinylacetylene was purified by distillation. The colloidal palladium was prepared on gum arabic and contained about 1 mg of Pd in 1 ml of solution. All the experiments were carried out with the same sample of catalyst. The hydrogen was obtained by electrolysis of 30% sodium hydroxide solution and purified in the usual way. The hydrogenation was carried out in a long-necked, pear-shaped flask with a side inlet passing into the flask. Into the flask was placed 20 ml of ethyl alcohol, 5 ml of colloidal palladium and the organic additive. When the air had been flushed from the flask and the whole system, the side inlet was connected to a gasometer containing vinylacetylene over a saturated sodium chloride solution. With the tap of the gasometer closed, the reaction flask was evacuated by means of a mercury burette. A sample of vinylacetylene was withdrawn with the

TABLE 4

Hydrogenation in the Ratio of 1 : 0.5

Additives		Amount of vinylacetylene taken (in ml)	Amount of hydrogen absorbed (in ml)	Hydrogenation time (in min.)	Analysis of hydrogenation products				
					total amount of unsaturated hydrocarbons		percent composition of unsaturated hydrocarbons		
name	amount (in % of weight of vinylacetylene)				(in ml)	(in %)	vinylacetylene	butadiene	butylenes
Without additives		377.0	188.5	33	358	94.8	54.3	41.8	3.9
The same		382.0	191.0	36	352	92.0	50.2	46.6	3.2
Lead acetate	0.114	379.0	190.0	82	352	92.9	59.5	39.6	0.9
The same	0.118	364.6	182.3	79	344	94.2	59.3	40.7	0.0
Pyridine	11.2	383.0	191.5	32	349	91.1	44.3	49.2	6.5
The same	22.4	384.0	192.0	30	358	93.3	45.6	42.8	11.6
Quinoline	11.2	386.0	193.0	37	363	94.0	55.3	43.5	1.2
Diethylamine	3.9	390.0	195.0	49	363	93.1	48.0	42.0	10.0
The same	7.9	384.0	192.0	79	346	90.2	47.1	41.5	11.4

reaction flask shaken. The hydrogenation was carried out with the flask shaken at 120 vibrations per minute. At the end of the experiment, the side outlet of the flask was connected to a gasometer containing a saturated solution of sodium chloride and the gas mixture flushed into the gasometer with hydrogen. Then, with the side outlet and the neck of the flask tightly closed, it was transferred to a vertical water condenser, whose upper end was connected to a gasometer. The neck of the flask was tightly attached to the lower end of the condenser. The side outlet of the flask was attached to a dropping funnel, from which 80-100 ml of a saturated solution of sodium chloride was introduced into the flask with heating. The flask was heated until the evolution of gas ceased. After this, the contents of the flask were flushed out with air. The whole of the gas mixture, which was usually 800-900 ml, was analyzed quantitatively.

The total content of unsaturated hydrocarbons in the gas mixture was determined with bromine water in absorption bulb pipettes [6]. The vinylacetylene content was determined with an alkaline solution of mercuric iodide and potassium iodide [7]. The butadiene content was determined in A. A. Korotkov's apparatus [8]. The amount of butylenes was calculated by the difference between the total content of unsaturated hydrocarbons and the total of butadiene and vinylacetylene.

The work was carried out at room temperature (17-22°) and atmospheric pressure (749-780 mm).

The results of the experiments are presented in Tables 2-4. All the gas volumes in the tables are reduced to normal conditions with a correction for the vapor pressure of water. Lead and copper acetates, pyridine, and ethylamine were used in aqueous solutions. The other additives were in alcohol solution.

SUMMARY

1. The hydrogenation of vinylacetylene in the presence of colloidal palladium with various additives was studied with ratios of vinylacetylene to hydrogen of 1:1, 1:0.75, and 1:0.5 (in moles).

2. It was established that in the hydrogenation of vinylacetylene without additives, at any ratio butylenes and butane were formed together with a predominant amount of butadiene. The amount of the former fell sharply in hydrogenation with a ratio of vinylacetylene to hydrogen of 1:0.5.

3. Lead and copper acetates slowed the hydrogenation reaction, increased the yield of butadiene, and decreased the butylene content.

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HYDROGENATION OF UNSATURATED COMPOUNDS IN THE PRESENCE OF COLLOIDAL PALLADIUM

XII. HYDROGENATION OF ALKYLACETYLENES AND PHENYLACETYLENE

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In a series of works it was shown that in contrast to hydroxy derivatives of disubstituted acetylenes, alcohols with a terminal acetylene grouping are hydrogenated quite selectively in the presence of palladium (colloidal or precipitated on calcium carbonate), i.e., the first mole of hydrogen is added exclusively at the triple bond [1-4]. Alkenylacetylenes behave similarly, while vinylalkylacetylenes are hydrogenated much less selectively [5].

It seemed interesting to study the hydrogenation of monosubstituted acetylene hydrocarbons with alkyl and aryl radicals on colloidal palladium under the same conditions. For this purpose, we investigated hexyne-1, heptyne-1, octyne-1, and phenylacetylene. It was found that all these hydrocarbons added the first two atoms of hydrogen at almost constant rate and then the rate increased sharply and again fell, as indicated in the figure. The hydrogenation curves of alkylacetylenes showed a marked similarity to the hydrogenation curves of alkenylacetylenes [5]. With phenylacetylene, the increase in reaction rate in the second stage of the process was expressed less sharply (see figure).

In this respect, our observations agree to a certain extent with the conclusions of other authors [6-9].*

Alkylacetylenes added the first molecule of hydrogen quite selectively. Samples taken directly from the reaction mass did not give a precipitate with an ammoniacal solution of silver oxide. The hydrogenation products were isolated and distilled and did not show the presence of an acetylene bond by the infrared spectrum (the frequencies of a terminal acetylene grouping at about 2120 and 3300 cm^{-1} were absent from the spectra). The bromide–bromate method indicated the presence of 95-98% of compounds with a double bond. In physical constants, the hydrocarbons obtained corresponded to corresponding olefins. As was expected, the infrared spectra of the hydrogenation products showed the characteristic frequencies of a vinyl group, for example, in the case of the hydrogenation of octyne-1, the frequencies 1649, 993, and 911 cm^{-1}.

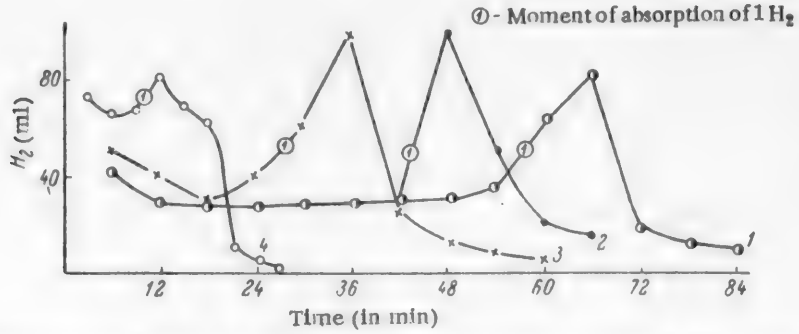
In the hydrogenation of phenylacetylene on colloidal palladium with a ratio of 1 mole of hydrogen to 1 mole of hydrocarbon, Kelber and Schwartz [6] obtained mainly styrene. There are no quantitative data in their communication. In our experiments on the hydrogenation of phenylacetylene in a molar ratio of hydrogen, judging by the infrared spectrum (the frequencies of 2120 and 3300 cm^{-1} were absent from the spectra)** and the reaction with ammoniacal silver oxide, the product isolated (88.5%) did not contain a substance with an acetylene bond and

*The very low rate of hydrogenation of phenylacetylene in the work of Hungarian chemists [9] is surprising – 0.2 g of substance in the presence of 1.5 ml of colloidal palladium added half of the theoretical amount of hydrogen (46 ml) after 18 hours. In Yu. S. Zal'kind's work [7] and ours, the hydrogenation rate of phenylacetylene was hundreds of times greater.

**We are grateful to T. V. Yakovleva for plotting and interpreting the infrared spectra.

contained 97.7% of a compound with a double bond according to the bromide–bromate method. Hydrogenation of the phenyl nucleus after saturation of the side radical, which was noted by Yu. S. Zal'kind [7], was not observed in our experiments.

Thus, it was shown that monosubstituted acetylene hydrocarbons with alkyl and phenyl radicals addhydrogen quite selectively at the triple bond over colloidal palladium.



Hydrogenation curves of monosubstituted acetylene hydrocarbons. 1) Hexyne-1, 2) heptyne-1, 3) octyne-1, 4) phenylacetylene.

EXPERIMENTAL

The alkylacetylenes were obtained by the action of appropriate bromides on sodium acetylide in liquid ammonia [10]. Their constants agreed with literature data [11]:

	B.p.	d_4^{20}	n_D^{20}
Hexyne-1	70—71°	0.716	1.3984
Heptyne-1	99—100	0.733	1.4064
Octyne-1	126.5	0.746	1.4159

Phenylacetylene was obtained from styrene through dibromostyrene in 57-60% yield (b.p. 142-143°, d^{20}_4 0.930, $n^{20}D$ 1.5501). The hydrogen was obtained by electrolysis of alkali. The hydrogenation was carried out in a pear-shaped flask at room temperature and atmospheric pressure. For all the experiments we used one sample of colloidal palladium, containing 2 mg of Pd in 1 ml of solution. Its activity was checked on tetramethylbutynediol. The experimental data on exhaustive hydrogenation are presented in Table 1.

TABLE 1

Exhaustive Hydrogenation of Acetylene Hydrocarbons

Hydrocarbons	Amt. of hydrocarbon (in g)	Calc. amt. of hydrogen (in ml)	Pressure (in mm)	Amt. of hydrogen (in ml) added in time (in minutes)									
				12	24	36	48	60	72	84	96	110	140
Hexyne-1	0.961	583	751	74	131	186	248	349	449	474	496	517	565
Heptyne-1	0.960	484	763	75	132	193	322	400	431	453	471	484	—
Octyne-1	0.995	445	760	101	182	342	381	396	404	410	417	442	—
Phenylacetylene-1	0.961	462	761	293	446	452	454	455	455	455	—	—	—

Footnote: The hydrocarbon was about 0.01 mole with 30 ml of methanol and 3 ml of palladium solution at 20° and with 120 vibrations of the flask per minute.

TABLE 2

Hydrogenation of Hydrocarbons at a Molar Ratio of 1:1

Hydrocarbons	Amt. of hydrocarbon (in g)	Amt. of hydrogen (in ml)	Pressure (in mm)	Hydrogenation time (in minutes)	Yield of hydrogenation products (in %)	Compounds with a double bond detected in the hydrogenation products (in %)
Hexyne-1	8.1	2460	751	150	73.3	97.7
Heptyne-1	10.31	2681	752	150	86.5	98.8
Octyne-1	7.75	1769	742	107	83.9	95.9
Phenylacetylene	8.22	2006	761	55	88.5	97.7

Footnote: 1. To exclude possible polymerization of styrene, a small amount of Neozone was introduced into the flask in the hydrogenation of phenylacetylene. 2. The amount of colloidal palladium was 10 ml, methanol, 70 ml, and the temperature 20°.

In experiments on the hydrogenation of acetylene hydrocarbons in a molar ratio (Table 2), after the hydrogenation, an equal volume of water was added to the reaction mixture with external cooling and the hydrogenation products obtained were steam distilled. The hydrocarbons were salted out from the distillate with a saturated solution of calcium chloride and then distilled and analyzed (Table 3).

TABLE 3

Properties of Hydrogenation Products Obtained

Hydrocarbons	Boiling points	d_{20}^{4}	n_D^{20}
Hexene-1	63— 64°	0.673	1.3880
Heptene-1	93— 94	0.696	1.3988
Octene-1	120—121	0.717	1.4083
Styrene	144—145	0.912	1.5429

SUMMARY

1. A study was made of the hydrogenation of some monoalkylacetylenes and phenylacetylene with colloidal palladium in methanol solution.

2. It was established that the hydrogenation proceeds strictly selectively at the triple bond to form the corresponding olefins and styrene.

3. The hydrogenation rate increases sharply after the addition of the first two atoms of hydrogen and then falls again.

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POLYENE COMPOUNDS

IX. CONDENSATION OF ACETALS OF CINNAMALDEHYDE, FURFURALDEHYDE AND FURYLACRYLALDEHYDE WITH UNSATURATED ETHERS

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On a series of examples, we previously [1, 2] showed that the acetals of aromatic aldehydes and ketones react with unsaturated ethers to form the corresponding ethoxy derivatives, which could be used for the preparation of α,β-unsaturated aldehydes.

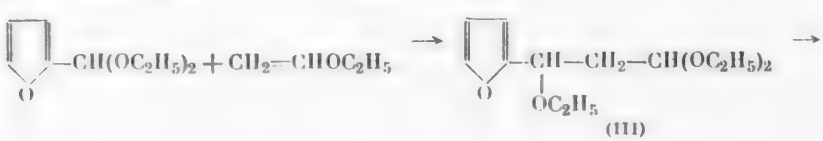
In the present work, which is a continuation of these investigations, the condensations of the diethyl acetals of cinnamaldehyde, furfuraldehyde, and furylacrylaldehyde with vinyl ethyl ether and 1-ethoxybutadiene-1,3 were studied.

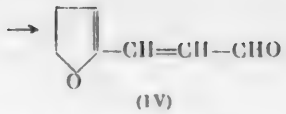
The reaction of the diethyl acetals of these aldehydes with α,β-unsaturated ethers proceeded readily in the presence of an acetic acid solution of zinc chloride and led to the formation of the corresponding ethoxy derivatives of the aromatic and furan series, which were then smoothly converted into unsaturated aldehydes by boiling with acetic acid [3]. In the case of reaction between the diethyl acetals of cinnamaldehyde, furfuraldehyde and furylacrylaldehyde with vinyl ethyl ether, even with an equimolecular ratio of the reagents, the products of the condensation of the acetal with one molecule of vinyl ethyl ether were obtained in good yields. Hardly any products of the addition of two, three etc. molecules of vinyl ethyl ether were formed, which is explained by the considerably lower reactivity of the acetal ethoxyl groups in the acetals obtained in comparison with the ethoxyl groups of the original acetals. Thus, the diethyl acetal of cinnamaldehyde reacted with vinyl ethyl ether to form 5-phenyl-1,1,3-triethoxypentene-4 (I). When boiled with glacial acetic acid, 5-phenyl-1,1,3-triethoxypentene-4 was converted in good yield into 5-phenylpentadiene-2,4-al (II). This procedure may be used as a preparative method for obtaining this aldehyde, which was previously obtained [4] by condensation of acetaldehyde with cinnamaldehyde in poor yield.

$$C_6H_5CH{=}CH{-}CH(OC_2H_5)_2 + CH_2{=}CHOC_2H_5 \rightarrow$$

$$\rightarrow C_6H_5CH{=}CH{-}\underset{\displaystyle OC_2H_5}{\underset{|}{CH}}{-}CH_2{-}CH(OC_2H_5)_2 \;(\text{I}) \rightarrow C_6H_5CH{=}CH{-}CH{=}CH{-}CHO \;(\text{II})$$

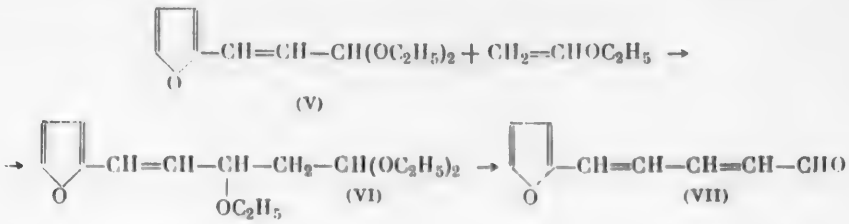
The reaction between the diethyl acetal of furfuraldehyde and vinyl ethyl ether also proceeded readily with the formation of 3-(furyl-2)-1,1,3-triethoxypropane (III). In this case, we mainly obtained the condensation product of the diethyl acetal of furfuraldehyde with one molecule of vinyl ethyl ether. When boiled with acetic acid, 3-(furyl-2)-1,1,3-triethoxypropane was converted into β-(furyl-2)-acrolein (IV), which was previously synthesized from furfuraldehyde and acetaldehyde [5].





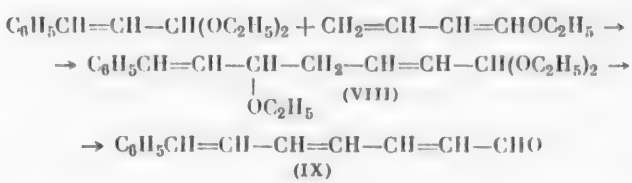
(IV)

To prepare 5-(furyl-2)-pentadiene-2,4-al, which was formed from furfuraldehyde and acetaldehyde in low yield [5], we reacted the diethyl acetal of β-(furyl-2)-acrolein (V) with vinyl ethyl ether. With an equimolecular ratio between the starting materials, we obtained a good yield of 5-(furyl-2)-1,1,3-triethoxypentene-4 (VI), which was converted into 5-(furyl-2)-pentadien-2,4-al (VII) by boiling with acetic acid.



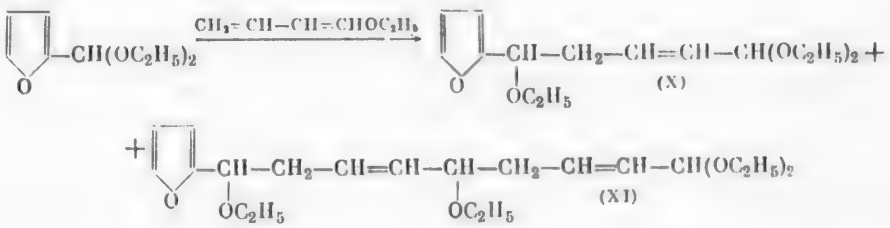
(V) (VI) (VII)

The condensation of acetals of cinnamaldehyde, furfuraldehyde, and furylacrylaldehyde with 1-ethoxybutadiene-1,3 was of particular interest as it made it possible to lengthen the carbon chain by four, eight, and more carbon atoms in one stage. In contrast to the reaction with vinyl ethyl ether, the reactions of the acetals of these aldehydes with 1-ethoxybutadiene-1,3 did not stop at the addition of one molecule of ethoxydiene. In some cases, doubling the amount of acetal made it possible to increase the yield of the primary condensation product. Thus, by interaction of twice the amount of the diethyl acetal of cinnamaldehyde with 1-ethoxybutadiene-1,3, we obtained 7-phenyl-1,1,5-triethoxyheptadiene-2,6 (VIII) in 63% yield, calculated on the acetal reacting. When boiled with acetic acid, 7-phenyl-1,1,5-triethoxyheptadiene-2,6 was converted into 7-phenylheptatrien-2,4,6-al (IX). The formation of this aldehyde indicated that 1-ethoxybutadiene-1,3 was added to the diethyl acetal of cinnamaldehyde in the 1,4-position.



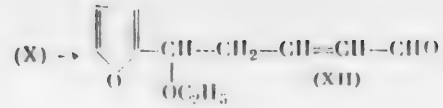
(VIII) (IX)

Interaction of the diethylacetal of furfuraldehyde with 1-ethoxy-butadiene-1,3 led to the formation of two compounds: 5-(furyl-2)-1,1,5-triethoxypentene-2(X) and 9-(furyl-2)-1,1,5,9-tetraethoxynonadiene-2,6 (XI).

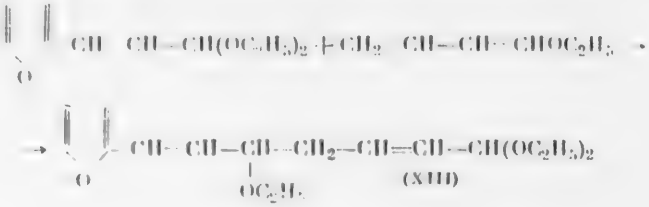


(X) (XI)

While 5-(furyl-2)-1,1,3-triethoxypentene-4 (VI) was converted into 5-(furyl-2)-pentadien-2,4-al (VII) in good yield when boiled with glacial acetic acid for 30 minutes, 5-(furyl-2)-1,1,5-triethoxypentene-2 (X) was mainly converted into 5-(furyl-2)-5-ethoxypenten-2-al (XII) under the same conditions. Apparently, the ethoxyl group of acetal (VI) in position 3 was more labile than the ethoxyl group in position 5 in acetal (X), where there was no activating effect from the double bond in the side chain.



The diethylacetal of β-(furyl-2)-acrolein condensed with 1-ethoxybutadiene-1,3 in the presence of boron trifluoride with the formation of 7-(furyl-2)-1,1,5-triethoxyheptadiene-2,6 (XIII).



EXPERIMENTAL

5-Phenyl-1,1,3-triethoxypentene-4 (I). To a mixture of 41.2 g of the diethyl acetal of cinnamaldehyde and 2 ml of a 10% acetic acid solution of zinc chloride, heated to 50°, was added 14.8 g of vinyl ethyl ether at such a rate that the temperature did not rise above 50°. The reaction mixture was kept at 49-51° for 1 hour, cooled to room temperature and shaken with 40 ml of a 10% solution of NaOH and 40 ml of diethyl ether. Removal of the ether and fractionation of the residue yielded 48.5 g (87.2%) of 5-phenyl-1,1,3-triethoxypentene-4.

B.p. 157-159° (3 mm), $d^{21.5}_4$ 0.9730, $n^{21.5}D$ 1.5010, MR 84.28; calc. 81.88.
Found %: C 73.04, 72.86; H 9.40, 9.24 $C_{17}H_{26}O_3$. Calculated %: C 73.36; H 9.40.

5-Phenylpentadiene-2,4-al (II). A mixture of 25 g of 5-phenyl-1,1,3-triethoxypentene-4 (I), 38 ml of glacial acetic acid and 3.8 ml of sodium acetate was boiled for 3 hours in a stream of nitrogen. The mixture was cooled to room temperature, 75 ml of water and 40 g of sodium carbonate added and the aldehyde extracted with ether. Removal of the ether and fractionation of the residue in vacuum yielded 10.8 g (76 %) 5-phenylpentadien-2,4-al. The b.p. was 134-135° (2 mm) and the m.p. 37-38° [4].

The 2,4-dinitrophenylhydrazone had m.p. 200-202°.

Found %: C 60.21, 60.02; H 3.95, 3.95; N 16.81, 16.85. $C_{17}H_{14}O_4N_4$. Calculated %: C 60.35; H 4.17; N 16.56.

3-(Furyl-2)-1,1,3-triethoxypropane (III). To 34 g of the diethyl acetal of furfuraldehyde was added 1 ml of a 10% acetic acid solution of zinc chloride and then at 20-23°, 14.4 g of vinyl ethyl ether was introduced. The reaction was carried out as described in the previous experiment. We obtained 8.3 g of the starting diethyl acetal of furfuraldehyde and 27.1 g (74.7% on the acetal reacting) of 3-(furyl-2)-1,1,3-triethoxypropane.

B.p. 124-125° (10 mm), d^{20}_4 0.9899, $n^{20}D$ 0.4470, MR 65.40; calc. 65.67.
Found %: C 64.32; 64.32; H 9.17, 9.10. $C_{13}H_{22}O_4$. Calculated %: C 64.46; H 9.09.

β-(Furyl-2)-acrolein (IV). A mixture of 22.7 g of 3-(furyl-2)-1,1,3-triethoxypropane, 35 ml of glacial acetic acid, and 3.5 g of sodium acetate was boiled for 1 hour in a stream of nitrogen. The usual treatment yielded 9.3 g (82%) of β-(furyl-2)-acrolein with m.p. 47-49°. After recrystallization from a mixture of hexane and benzene, the substance melted at 52-53° [5].

Diethyl acetal of β-(furyl-2)-acrolein (V). A mixture of 21.1 g of β-(furyl-2)-acrolein, 29.6 g of orthoformic ester, 65 ml of anhydrous alcohol and 0.35 g of ammonium chloride was left to stand at room temperature for three days. The solution was diluted with water and extracted with ether. Removal of the ether and fractionation in vacuum yielded 16.5 g (48.7%) of the diethyl acetal of β-(furyl-2)-acrolein (V).

B.p. 98-99° (3 mm), d^{20}_4 1.0053, $n^{20}D$ 1.4920 [6], MR 56.63; calc. 54.32.

5-(Furyl-2)-1,1,3-triethoxypentene-4 (VI). To a mixture of 27.6 g of the diethyl acetal of β-(furyl-2)-acrolein and 0.7 ml of a 10% acetic acid solution of zinc chloride was added 9.8 g of vinyl ethyl ether at room temperature. The reaction mixture was kept at room temperature for 1.5 hours and treated in the usual way. We obtained 24.1 g (74.6% on the acetal reacting) of 5-(furyl-2)-1,1,3-triethoxypentene-4.

B.p. 135-137° (2 mm), d^{20}_4 0.9937, $n^{20}D$ 1.7490, MR 76.55; calc. 74.59.
Found %: C 67.12, 66.93; H 9.04, 8.97. $C_{23}H_{24}O_4$. Calculated %: C 67.14; H 9.01.

5-(Furyl-2)-pentadien-2,4-al (VII). A mixture of 10.7 g of 5-(furyl-2)-1,1,3-triethoxypentene-4 (VI), 14 ml of glacial acetic acid and 1.4 g of sodium acetate was boiled in a stream of nitrogen for 30 minutes. The usual treatment and recrystallization of the substance from ligroine yielded 3.1 g (52.6%) of 5-(furyl-2)-pentadien-2,4-al with m.p. 68-69° [5]. The 2,4-dinitrophenylhydrazone had m.p. 222-223°.

Found %: C 54.82, 54.95; H 3.68, 3.97. $C_{15}H_{12}O_5N_4$. Calculated %: C 54.88; H 3.68.

7-Phenyl-1,1,5-triethoxyheptadiene-2,6 (VIII). To a mixture of 56.1 g of the diethyl acetal of cinnamaldehyde and 0.6 g of a 10% solution of zinc chloride in acetic acid was added 14.6 g of 1-ethoxybutadiene-1,3 at room temperature. The reaction mixture was kept at the same temperature for 1 hour and shaken with 10% sodium carbonate solution. The product was extracted with ether. Removal of the ether and fractionation of the residue yielded 22.4 g (63.4% on the acetal reacting) of 7-phenyl-1,1,3-triethoxyheptadien-2,4-al.

B.p. 192-194° (4 mm), d^{20}_4 0.9764, $n^{20}D$ 1.5112, MR 93.43; calc. 90.37.
Found %: C 74.98, 75.19; H 9.22, 9.24. $C_{19}H_{28}O_3$. Calculated %: C 74.96; H 9.27.

7-Phenylheptatrien-2,4,6-al (IX). A mixture of 1.3 g of 7-phenyl-1,1,3-triethoxyheptadiene-2,6, 7 ml of acetic acid, and 0.3 g of sodium acetate was boiled for 1 hour in a stream of nitrogen. The reaction mixture was treated as described above and the aldehyde extracted with ether. Purification by vacuum distillation and recrystallization from ligroine yielded 0.15 g of 7-phenylheptatrien-2,4,6-al with m.p. 116° [7].

5-(Furyl-2)-1,1,5-triethoxypentene-2 (X) and 9-(furyl-2)-1,1,5,9-tetraethoxynonadiene-2,6 (XI). 9.8 g of 1-ethoxybutadiene-1,3 was added dropwise to a mixture of 34 g of the diethyl acetal of furfuraldehyde and 0.5 ml of a 10% acetic acid solution of zinc chloride. The reaction was carried out as described above. We obtained 27.5 g of the original diethyl acetal of furfuraldehyde with b.p. 65-69° (10 mm) and 2.4 g of 5-(furyl-2)-1,1,5-triethoxypentene-2 (X) (23.7% on the acetal reacting).

B.p. 124-126° (2 mm), d^{20}_4 0.9857, $n^{20}D$ 1.4612; MR 74.30; calc. 74.59.
Found %: C 66.81, 67.06; H 9.00, 9.04. $C_{15}H_{24}O_4$. Calculated %: C 67.14; H 9.01.

In addition, we also isolated 3.4 g (24.7% on the acetal reacting) of 9-(furyl-2)-1,1,5,9-tetraethoxynonadiene-2,6 (XI).

B.p. 193-197° (4 mm), d^{20}_4 0.9212, $n^{20}D$ 1.4697, MR 104.1; calc. 103.8.
Found %: C 68.51, 68.63; H 9.18, 9.16. $C_{21}H_{34}O_5$. Calculated %: C 68.82; H 9.35.

2,4-Dinitrophenylhydrazone of 5-(furyl-2)-5-ethoxypenten-2-al (XII). A mixture of 3.7 g of 5-(furyl-2)-1,1,5-triethoxypentene-2 (X), 5 ml of glacial acetic acid, and 0.5 g of sodium acetate was boiled for 30 minutes in a stream of nitrogen. The usual processing yielded 1.6 g of a substance with b.p. 120-125° (6 mm). The addition of 2,4-dinitrophenylhydrazine hydrochloride to an alcohol solution of this substance yielded 0.08 g of the 2,4-dinitrophenylhydrazone of 5-(furyl-2)-pentadien-2,4-al with b.p. 219-221° (a mixed melting point with the sample previously obtained was not depressed) and 0.26 g of the 2,4-dinitrophenylhydrazone of 5-(furyl-2)-5-ethoxypenten-2-al (XII) with m.p. 143-144° (from alcohol).

Found %: C 55.05; H 4.81; N 15.14. $C_{17}H_{18}O_6N_4$. Calculated %: C 54.54; H 4.84; N 14.97.

7-(Furyl-2)-1,1,5-triethoxyheptadiene-2,6 (XIII). To a mixture of 29.1 g of the diethyl acetal of β-(furyl-2)-acrolein and 0.8 g of boron trifluoride etherate at 0-3° was added 7.41 g of 1-ethoxybutadiene-1,3. The reaction mixture was kept at the same temperature for 30 minutes and treated as described above. Removal of the ether and fractionation of the residue yielded 8.8 g (40.4%) of 7-(furyl-2)-1,1,5-triethoxyheptadiene-2,6.

B.p. 148-151° (3 mm), d^{20}_4 0.9941, $n^{20}D$ 1.4928, MR 86.03; calc. 83.11.
Found %: C 69.67, 69.67; H 8.98, 9.00. $C_{17}H_{26}O_4$. Calculated %: C 69.36; H 8.90.

SUMMARY

1. It was shown that the condensation of the diethyl acetals of cinnamaldehyde, furfuraldehyde and furylacrylaldehydes with vinyl ethyl ether and 1-ethoxybutadiene-1,3 yielded the corresponding phenyl- and furylethoxyalkenes, which were converted into saturated aldehydes by boiling with acetic acid.

2. A simple method of preparing 5-phenylpentadien-2,4-al was found, based on the condensation of the diethyl acetal of cinnamaldehyde with vinyl ethyl ether.

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STUDY OF THE REACTIVITY OF α- AND β-OXIDES OF β-SITOSTEROL

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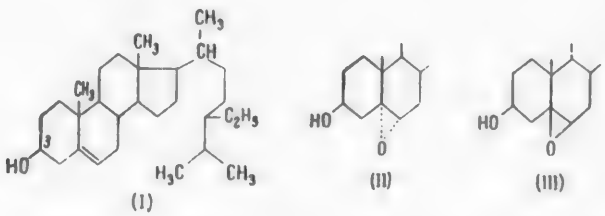
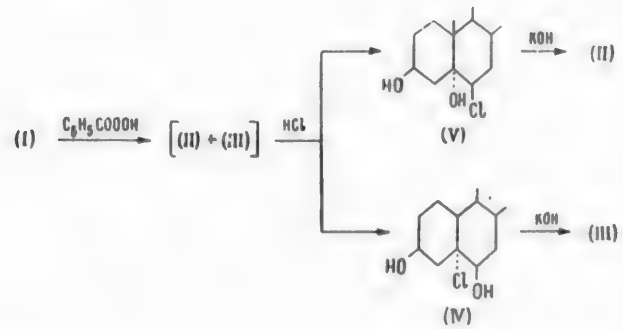
On the basis of the structure of β-sitosterol (I), it was to be expected that it would form two isomeric oxides, (II) and (III) on oxidation:



(I) (II) (III)

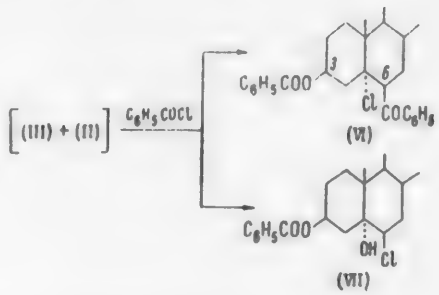
However, after treating it with benzoyl hydroperoxide, we were able to isolate only one substance with m.p. 148-150°. Similarly, oxidation of the 3-acetate of β-sitosterol yielded an oxide acetate with m.p. 160-162°. Attempts to resolve the oxides by many recrystallizations from alcohol or by chromatographic adsorption on aluminum oxide did not lead to the desired results and only by the action of gaseous hydrogen chloride on a chloroform solution of the oxide with m.p. 148-150° were we able to isolate isomeric chlorodiols with m.p. 214-214.5° (IV) and 177-179° (V). Treatment of the latter with an alcohol solution of potassium hydroxide yielded substances with m.p. 230-232° and 141-142°, which corresponded to oxides of sitosterol according to elementary composition. By the action of gaseous hydrogen chloride on a chloroform solution of the 3-acetate of β-sitosterol oxide we also isolated two substances with m.p. 203-205° and 194-195°, which were found to be chlorohydrins of the acetates mentioned.

Thus, the following processes occurred during the oxidation of β-sitosterol (I) and subsequent hydrochlorination and also dehydrochlorination:

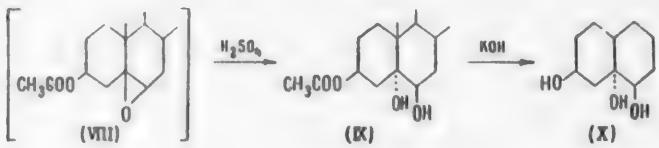


The interaction of the β-sitosterol oxides and also their acetyl derivatives with benzoyl chloride yielded substances with m.p. 205-206.5, 210-212°, 196-198° and 203-205°. The first two refer to the 3β,6β-dibenzoate

of 5-chloro-(VI) and the 3β-benzoate of 5-hydroxy-6β-chloro-β-sitostane (VII) respectively, since the compounds were isolated from the 3-hydroxy derivative; the second two compounds, which were synthesized from the 3β-acetylated oxides, were the 3β-acetate of the 5-chloro-6β-benzoate and the 3β-acetate of 5-hydroxy-6β-chloro-β-sitostane.



The interaction of the 3-acetate of β-sitosterol oxide (VIII) with 20% sulfuric acid, even at normal temperature, gradually produced opening of the oxide ring with the formation of the 3β-acetate of 5,6β-dihydroxy-β-sitostane with m.p. 216-218° (IX), which was converted into 3β,5,6β-trihydroxy-β-sitostane (X) by hydrolysis with an alcohol solution of potassium hydroxide.



On comparing the behavior of β-sitosterol oxides with those of cholesterol [1], it is possible to see a certain analogy with the oxides of the latter; the α-oxide ring is cleaved at C_6, while the β-oxide ring is cleaved at C_5. As with other oxides, Walden inversion occurs at the carbon atom of the C—O bond which is cleaved; the same inversion occurs during closure of the oxide ring. We accepted the position of rupture of the oxide ring in analogy with the action of hydrogen chloride on cholesterol oxides [2].

EXPERIMENTAL

α- and β-Oxides of β-sitosterol. To a solution of 50 g of β-sitosterol (m.p. 136-137°) in 500 ml of chloroform at −10° was added 354 ml of a chloroform solution of benzoyl hydroperoxide (1 ml of solution contained 0.057 g of hydroperoxide) from a dropping funnel with continuous stirring. When the chloroform solution had been stirred for one hour and kept at −10° for 16 hours, it was washed in a separating funnel with 5% sodium carbonate solution and dried over anhydrous sodium sulfate, the solvent removed in vacuum and the residue recrystallized from alcohol. We obtained 36 g of a substance with m.p. 148-150°, which formed lustrous, colorless platelets that were sparingly soluble in alcohol in the cold and readily so on heating and readily soluble in ether.

Found %: C 80.51, 80.65; H 11.88, 12.06. $C_{29}H_{50}O_2$. Calculated %: C 80.93, H 11.61.

α- and β-Oxides of β-sitosterol 3-acetate. A similar oxidation to the previous one with 50 g of β-sitosterol 3-acetate (m.p. 121-122°) in 450 ml of chloroform and 222 ml of a chloroform solution of benzoyl hydroperoxide (1 ml of solution contained 0.082 g of hydroperoxide) yielded 50.5 g of a substance with m.p. 121-122°, which melted at 160-162° after recrystallization from alcohol. The colorless, plate-like crystals were sparingly soluble in cold alcohol, more so in hot alcohol, and soluble in ether.

Found %: C 78.46, 78.70; H 11.30, 11.51. $C_{31}H_{52}O_3$. Calculated %: C 78.81; H 11.02.

3β,6β-Dihydroxy-5-chloro- and 3β,5-dihydroxy-6β-chloro-β-sitostanes. 10 g of β-sitosterol oxide (m.p. 148-150°) was dissolved in 500 ml of dry chloroform and a stream of dry hydrogen chloride passed through the solution for 2.5 hours (a brownish red color was observed). After a day, the precipitate formed was collected, washed with water and dried. We obtained 4.18 g of a halogen-containing substance (Beilstein test), which melted at 214-214.5° after recrystallization from alcohol and a mixture of ethyl acetate and methanol (1:1).

Found %: C 73.90, 74.07; H 10.09, 10.49; Cl 7.74, 7.66. $C_{29}H_{51}O_2Cl$. Calculated %: C 74.59; H 10.93; Cl 7.78.

Removal of the chloroform from the mother solution yielded 4 g of a substance, which melted at 177-179° after being washed with water and recrystallized from a mixture of ethyl acetate and methanol (1.4 g was obtained). The white needle-like crystals were insoluble in water, but soluble in alcohol.

Found %: C 74.99, 74.56; H 11.35, 11.11; Cl 7.33, 7.46. $C_{29}H_{51}O_2Cl$. Calculated %: C 74.59; H 10.93; Cl 7.78.

β-Sitosterol α-oxide. 0.3 g of 3β,5-dihydroxy-6β-chloro-β-sitostane (m.p. 177-179°) was heated under reflux on a water bath with 10 ml of a 0.5 N alcohol solution of potassium hydroxide for 1.5 hours. After concentration of the solution, the crystals precipitated were collected, washed with water, and recrystallized from alcohol. We obtained 0.15 g of a substance with m.p. 141-142°.

Found %: C 81.38, 80.96; H 12.19, 11.82. $C_{29}H_{50}O_2$. Calculated %: C 80.93; H 11.61.

β-Sitosterol β-oxide. This was obtained by analogous treatment of 0.3 g of 3β,6β-dihydroxy-5-chloro-β-sitostane with m.p. 214-214.5°. We isolated 0.1 g of substance with m.p. 230-232°.

Found %: C 81.20, 81.59; H 11.84, 11.99. $C_{29}H_{50}O_2$. Calculated %: C 80.93; H 11.61.

3β-Acetoxy-5-hydroxy-6β-chloro and 3β-acetoxy-5-chloro-6β-hydroxy-β-sitostanes. 5 g of the 3-acetate of β-sitosterol oxide (m.p. 160-162°) was dissolved in 50 ml of dry chloroform and a stream of dry hydrogen chloride passed into the solution for 1.5 hours (a dirty green color was observed). After a day, the solvent was removed in vacuum and the dirty green residue recrystallized from a mixture of ethyl acetate and methanol (1 : 1). We obtained 0.8 g of a substance with m.p. 203-205°.

Found %: C 73.47, 73.23; H 10.68, 10.56; Cl 6.69, 6.69. $C_{31}H_{53}O_3Cl$. Calculated %: C 73.10; H 10.42; Cl 6.98.

The product isolated from the mother solution melted at 194-195° after 4 recrystallizations from alcohol.

Found %: C 72.95, 73.50; H 10.47, 10.71; Cl 6.75, 6.77. $C_{31}H_{53}O_3Cl$. Calculated %: C 73.10; H 10.42; Cl 6.98.

3β,6β-Dibenzoxy-5-chloro- and 3β-benzoxy-5-hydroxy-6β-chloro-β-sitostanes. 5 g of β-sitosterol oxide (m.p. 148-150°) was dissolved in 20 ml of dry pyridine, mixed with 16 ml of benzoyl chloride and the mixture heated on a water bath for two hours with continuous stirring. The reaction mixture was poured into 5% sodium carbonate solution, the product extracted with ether, the ether extracts washed with water and dried over anhydrous sodium sulfate, the solvent removed and the residue recrystallized from a mixture of ethyl acetate and methanol and finally from ethyl acetate. We obtained 0.45 g of a substance with m.p. 205-206.5°.

Found %: C 76.18, 76.52; H 9.04, 8.70; Cl 4.85, 4.70. $C_{43}H_{59}O_4Cl$. Calculated %: C 76.49; H 8.75; Cl 5.26.

The mother solution was concentrated and the substance isolated recrystallized from a mixture of ethyl acetate and methanol in the presence of activated charcoal. We obtained 0.3 g of a substance with m.p. 210.5-212°.

Found %: C 76.19, 75.91; H 9.65, 10.06; Cl 5.72, 5.84. $C_{36}H_{55}O_3Cl$. Calculated %: C 75.71; H 9.64; Cl 6.22.

3β-Acetoxy-5-chloro-6β-benzoxy- and 3β-acetoxy-5-hydroxy-6β-chloro-β-sitostanes. 5 g of the acetate of β-sitosterol oxide (m.p. 160-162°) was dissolved in 20 ml of dry pyridine, mixed with 16 ml of benzoyl chloride and then treated as in the previous experiment. We obtained 0.3 g of a substance with m.p. 196-198°.

Found %: C 76.28, 76.07; H 9.55, 8.89; Cl 6.14, 5.48. $C_{38}H_{57}O_3Cl$. Calculated %: C 76.45; H 9.55; Cl 5.95.

Concentration of the mother solution and recrystallization of the product isolated from a mixture of ethyl acetate and methanol in the presence of activated charcoal yielded 0.2 g of a substance with m.p. 203-205°.

Found %: C 73.62, 73.45; H 10.54, 10.64; Cl 7.25, 7.13. $C_{31}H_{53}O_3Cl$. Calculated %: C 73.10; H 10.42; Cl 6.98.

3β-Acetoxy-5,6β-dihydroxy-β-sitostane. A solution of 1 g of the 3-acetate of β-sitosterol oxide (m.p. 160-162°) in a mixture of 10 ml of dichloroethane and 60 ml of acetone was mixed with 5 ml of a 20% solution of sulfuric acid and the mixture kept at 20° for a week. The precipitate of unreacted starting material was removed by filtration, the filtrate diluted with water and extracted with ether, the ether extracts washed with sodium carbonate solution and water and dried over anhydrous sodium sulfate and the solvent removed. Recrystallization from a mixture of alcohol and water (1 : 1) yielded 0.1 g of a white, crystalline substance with m.p. 216-218°.

Found %: C 76.43, 76.18; H 11.44, 11.14. $C_{31}H_{54}O_4$. Calculated %: C 75.91; H 11.03.

3β,5,6β-Trihydroxy-β-sitostane. 0.3 g of 3β-acetoxy-5,6β-dihydroxy-β-sitostane with m.p. 216-218° was heated under reflux on a water bath with a 0.5 N alcohol solution of potassium hydroxide for 1 hour. The crystals which separated after concentration of the solution were collected and recrystallized from alcohol. We obtained 0.1 g of white crystals with m.p. 224-226.5°.

Found %: C 78.06, 78.12; H 11.92, 12.08. $C_{29}H_{52}O_3$. Calculated %: C 77.67; H 11.61.

SUMMARY

1. The behavior of benzoyl hydroperoxide toward β-sitosterol and its 3-acetyl derivative was studied and a mixture of isomeric α- and β-oxides and also their acetyl derivatives were isolated.

2. 5,6β- and 6β,5-chlorodiols of β-sitostane, the α- and β-oxides of β-sitosterol and also their acetyl derivatives were isolated by hydrochlorination and subsequent dehydrochlorination.

3. It was shown that the interaction of β-sitosterol oxides with benzoyl chloride formed both 3β,6β-dibenzoxy-5-chloro and also 3β-benzoxy-5-hydroxy-6β-chloro-β-sitostanes; from the 3β-acetate of β-sitosterol oxide we obtained 3β-acetoxy-5-chloro-6β-benzoxy- and 3β-acetoxy-5-hydroxy-6β-chloro-β-sitostanes respectively.

4. It was shown that the interaction of the 3-acetate of β-sitosterol oxide with 20% sulfuric acid caused cleavage of the oxide ring with the formation of the 3-acetate of 5,6β-dihydroxy-β-sitostane and hydrolysis of the latter with potassium hydroxide formed 3β,5,6β-trihydroxy-β-sitostane.

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SYNTHESIS OF AROMATIC β-KETO ACETALS

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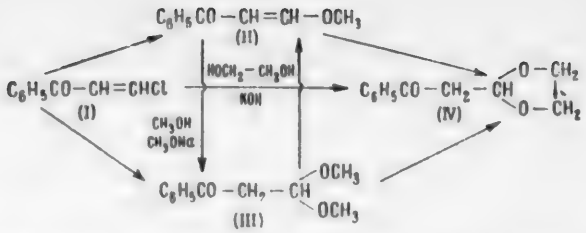
β-Keto acetals, which are mainly obtained from the corresponding β-chlorovinyl ketones [1], have found a variety of applications in organic synthesis in recent years. At the same time, representatives of this class containing aromatic radicals are almost completely unknown. There is only some information on the synthesis of the dimethyl and diethyl acetals of benzoylacetaldehyde [2-5]. The ethylene acetal of benzoylacetaldehyde was recently prepared in our laboratory [6]. Now we have developed a method of synthesizing various aryl-β-keto acetals on the basis of aryl β-chlorovinyl ketones, which have recently become readily available [7].

During the work we obtained two new representatives of this class, namely, o-tolyl and m-tolyl β-chlorovinyl ketones, and p-bromophenyl β-chlorovinyl ketone was also obtained for the first time by a direct method.

In the first attempts to synthesize the acetal of benzoylacetaldehyde under the conditions used for preparing aliphatic dimethyl acetals [1], we obtained, instead of the expected compound, another substance, which was found to be phenyl β-methoxyvinyl ketone (II). This complication compelled us to study the reaction considered in more detail. It was thus established that when phenyl β-chlorovinyl ketone [1] was added to an alcohol solution of an equivalent amount of alkali, the dimethyl acetal formed, but during the treatment which was first used and which consisted of removal of the mineral precipitate by filtration, evaporation of the methanol from the filtrate and vacuum distillation of the residual oil, a molecule of methyl alcohol was eliminated and phenyl β-methoxyvinyl ketone (II) was formed. The alcohol was apparently eliminated during the heating due to the catalytic effect of traces of alkali remaining in the filtrate. Elimination of alcohol under the action of alkali is also known for alkyl-β-keto acetals [8] and therefore, for the preparation of the acetal, the conditions were changed so as to exclude the presence of traces of alkali during the distillation. For this purpose, the reaction mixture was treated with water and extracted with ether. In this case the acetal of benzoylacetaldehyde (III) was obtained in 60% yield.

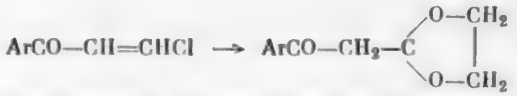
This reaction of the elimination of alcohol from the β-keto acetal during distillation is a reversible process since treatment of phenyl β-methoxyvinyl ketone (II) with methanol in the presence of sodium alcoholate again gave acetal (III) in high yield. Such ready interconvertibility of the acetal and the corresponding alkoxyvinyl ketone explains the relative instability of the β-keto acetal, of which there are many indications.

The ethylene acetals of β-keto aldehydes, which were recently synthesized in our laboratory [6], were much more convenient. Of representatives of the aromatic series, only the ethylene acetal of benzoylacetaldehyde (IV) is known. The considerably greater stability of cyclic ethylene acetals, which are readily obtained by the interaction of β-chlorovinyl ketones with ethylene glycol, is indicated by the fact that the latter are smoothly formed by treatment of both dimethyl acetals and alkoxyvinyl ketones with ethylene glycol in the presence of alkali. All the interconversions described above, which are connected with the investigation of the stability of benzoylacetaldehyde acetals, are represented by the scheme.



The best condensing agents for the synthesis of ethylene acetals of β-keto aldehydes of the aliphatic series are potassium hydroxide and potassium carbonate [6]. We tested their use and also that of sodium hydroxide in the synthesis of aromatic β-keto acetals. The yield of the ethylene acetal of benzoylacetaldehyde varied only insignificantly in relation to the alkali taken.

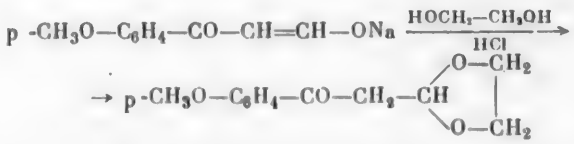
We then used the procedure developed for synthesizing the first member of the series for preparing ethylene acetals of β-keto aldehydes, substituted in the aromatic nucleus, and both potassium hydroxide and potassium carbonate were used as condensing agents. The yields of ethylene acetals of aroylacetaldehydes were 60-80%.



Ar-n, m, o-$CH_3C_6H_4$, p, o-ClC_6H_4, p-Br C_6H_4, p-$CH_3O—C_6H_4$.

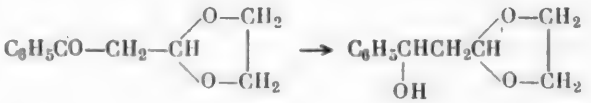
The acetals obtained were stable, crystalline, readily fusible substances, which were readily soluble in alcohol, benzene, and chloroform and less so in ligroine and petroleum ether; they did not give a color with ferric chloride solution, which is explained by their slow hydrolysis in contrast to the aliphatic analogs.

We also tested the possibility of synthesizing aromatic ethylene acetals from hydroxymethylene ketones [9] on the example of the preparation of the ethylene acetal of p-anisoylacetaldehyde:



It was found that in this reaction the yield was several times lower than the yield of the acetal obtained from the corresponding β-chlorovinyl ketone.

In conclusion, we attempted to convert β-keto acetals to indenol derivatives by cyclization of the corresponding acetal carbinols. By reduction of the ethylene acetal of benzoylacetaldehyde with lithium aluminum hydride, we obtained the ethylene acetal of β-hydroxy-β-phenylpropionaldehyde:



However, on treating the carbinol obtained with polyphosphoric acid in analogy with the synthesis of substituted naphthalenes developed in our laboratory [6, 10], we did not detect the formation of an indenol. As a result of this reaction, we isolated only cinnamaldehyde, which was identified as the semicarbazone.

EXPERIMENTAL

o-Tolyl-β-chlorovinyl ketone. This substance was obtained analogously to p-tolyl β-chlorovinyl ketone [7] from 65.7 g of o-toluyl chloride and 59.0 g of aluminum chloride in 220 ml of dry dichloroethane. The

reaction complex was prepared at 1-5° and acetylene passed for 5.5 hours at 48-50°. The yield was 50.5 g (66%). The b.p. was 105-107° (4 mm), $n^{20}D$ 1.5733, d^{20}_4 1.1612.

Found %: C 66.92, 67.00; H 5.16, 5.32. $C_{10}H_9OCl$. Calculated %: C 66.46; H 5.02.

m-Tolyl-β-chlorovinyl ketone. This compound was obtained as described above from 48.7 g of m-toluyl chloride and 43.5 g of aluminum chloride in 200 ml of dry dichloroethane. The reaction complex was prepared at 2-5° and acetylene passed for 7 hours 45 minutes at 45-52°. The yield was 31.6 g (55.7%). After three distillations, the m-tolyl β-chlorovinyl ketone had m.p. 14-15°, b.p. 101-103° (2 mm), n^{20}_4 1.5772, d^{20}_4 1.1529.

Found %: Cl 19.24, 19.29. $C_{10}H_9OCl$. Calculated %: Cl 19.63.

p-Bromophenyl β-chlorovinyl ketone. The substance was obtained as described above from 91.3 g of p-bromobenzoyl chloride in 230 ml of dry dichloroethane and 59.0 g of aluminum chloride. The reaction complex was prepared at 3-5° and acetylene passed for 5.5 hours at 45-48°. The yield was 78.6 g (77%). After redistillation, the p-bromophenyl β-chlorovinyl ketone had b.p. 135-138° (3 mm), m.p. 36-37°. According to data in [11]: m.p. 38.5-39.5°.

Found %: C 44.24, 44.37; H 2.49, 2.53. $C_{10}H_8OClBr$. Calculated %: C 44.18; H 2.44.

Phenyl β-methoxyvinyl ketone (II). With cooling and stirring, 81 g of phenyl β-chlorovinyl ketone was added dropwise to a solution of 20 g of sodium hydroxide in 220 ml of absolute methanol, the mixture kept for a day and then the precipitate removed by filtration, the methanol distilled from the filtrate and the residual oil vacuum distilled. The elimination of methanol was observed and a substance with b.p. 158-160° (20 mm) was obtained. The yield was 67 g (85%). After a second distillation, the phenyl β-methoxyvinyl ketone appeared as a colorless oil with a weak, fruity smell:

B.p. 159-160° (20 mm), $n^{20}D$ 1.5787, d^{20}_4 1.1040, MR_D 47.73; calc. 46.27.

According to data in [12]: b.p. 112° (2 mm), $n^{20}D$ 1.5777.

Found %: C 73.60, 73.70; H 6.47, 6.44. $C_{10}H_{10}O_2$. Calculated %: C 74.01; H 6.18.

Dimethyl acetal of benzoylacetaldehyde (III). a) From phenyl β-chlorovinyl ketone (I). The reaction was carried out with amounts of substances and under similar conditions to those described in the previous experiment. After the reaction the mixture was poured into water and extracted with ether, the ether extracts dried over sodium sulfate, the solvent removed and the residue vacuum distilled with a fraction with b.p. 111-113° (2 mm) collected. The yield was 57 g (60%). The colorless oil had a weak, fruity smell.

After a second distillation, the substance had the following constants:

B.p. 111-111.5° (2 mm), $n^{20}D$ 1.5103, d^{20}_4 1.0890, MR_D 53.34; calc. 52.80.

According to data in [5]: b.p. 90.5-93.5° (0.2 mm), $n^{20}D$ 1.5103.

Found %: C 68.04, 68.07; H 7.37, 7.37. $C_{11}H_{14}O_3$. Calculated %: C 68.03; H 7.20.

b) From phenyl β-methoxyvinyl ketone (II). To a solution of sodium alcoholate (from 0.02 g of sodium in 15 ml of anhydrous methanol) was added 8.1 g of phenyl β-methoxyvinyl ketone. The mixture was left for a day, then heated for 15 minutes at 60°, again left for 4 hours, treated with water and extracted with ether and the ether extract dried over sodium sulfate. The solvent was removed and the residue distilled to give a fraction with b.p. 117-118° (4 mm), $n^{20}D$ 1.5109. The yield was 7.3 g (76%).

Ethylene acetal of benzoylacetaldehyde (2-phenylacyl-1,3-dioxolane) (IV). a) From phenyl β-methoxyvinyl ketone (II). A mixture of 3 g of phenyl β-methoxyvinyl ketone with an equal volume of ethylene glycol, containing traces of potassium hydroxide, was stirred at room temperature for 8 hours and then for 20 minutes at 70°, left overnight, diluted with water and the precipitate collected and carefully washed with water on filter. The yield was 2 g (57%) and the m.p. 58.5–59°.

b) From the dimethyl acetal of benzoylacetaldehyde (III). To 1.3 g of the dimethyl acetal of benzoylacetaldehyde was added 3 ml of ethylene glycol, containing traces of potassium hydroxide; the mixture was stirred for 20 minutes at room temperature, then for 1 hour with heating on a water bath and finally left overnight. The acetal was isolated as described above. The yield was 1 g (77%) and the m.p. 58-58.5°.

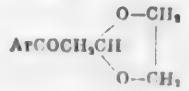
c) From phenyl β-chlorovinyl ketone (I). With stirring and cooling with water, 68.4 g of phenyl β-chlorovinyl ketone was added dropwise to a solution of 25 g of powdered potassium hydroxide in 300 ml of ethylene

glycol. Stirring was continued for 4 days and then the precipitate was collected and carefully washed on a filter with water and once with ether. The yield was 62.8 g (79%) and the m.p. 56-57°.

When sodium hydroxide was used, the yield was 70.5% and when potassium carbonate was used, 71.2%. After recrystallization from ligroine, all the samples of the ethylene acetal of benzoylacetaldehyde appeared as fine, white needles with m.p. 60-61°, which were identical according to mixed melting points. According to data in [6]: m.p. 58-59°.

Found %: C 68.88, 68.96; H 6.47, 6.51. $C_{11}H_{12}O_3$. Calculated %: C 68.74; H 6.30.

Ethylene acetals of aroylacetaldehydes. 1 mole of aryl β-chlorovinyl ketone was added dropwise, or in small portions for solid β-chlorovinyl ketones, to a solution of 1.1 mole of powdered potassium hydroxide (or baked potassium carbonate) in a large excess of ethylene glycol (10-15 moles). The mixture obtained was stirred for 3-4 days and then the precipitate was collected, washed with water on the filter and dried. Data on the aromatic ethylene β-keto acetals obtained by the method are presented in the table.

Ethylene Acetals of Aroylacetaldehydes 

No.	Ar	Yield (in %)		Melting point	Found (%)		Calculated (%)	
		with KOH	with K_2CO_3		C	H	C	H
1	p-$CH_3C_6H_4$	62	—	47.5—48.5°	69.95, 69.74	6.97, 6.90		
2	m-$CH_3C_6H_4$	—	75	48—49	70.17, 69.90	6.97, 6.87	69.92	6.80
3	o-$CH_3C_6H_4$	64	79	36—37	70.49, 70.43	6.93, 7.05		
4	p-ClC_6H_4	71	74	45—46	57.79, 57.88	5.03, 5.07	58.28	4.89
5	p-BrC_6H_4	82	69	55—56	49.22, 49.13	4.29, 4.27	48.72	4.09
6	o-ClC_6H_4	37	46	16—18*	58.43, 58.42	4.78, 5.03	58.28	4.89
7	p-$CH_3OC_6H_4$	64	—	66.5—67.5	64.96, 64.83	6.71, 6.60	64.85	6.37

*At room temperature the liquid had after 3 vacuum distillations b.p. 137-138° (2 mm), $n^{20}D$ 1.5852, d^{20}_4 1.2744, MR_D 56.23; calc. 55.36.

Ethylene acetal of p-anisoylacetaldehyde from p-methoxyacetophenone. To a suspension of 3.8 g of metallic sodium in 125 ml of anhydrous benzene was added 27 ml of anhydrous ethyl formate and then with stirring and cooling, a solution of 24 g of p-methoxyacetophenone in 25 ml of anhydrous benzene was added dropwise. The mixture gradually thickened and lightened. After 4 hours the precipitate was collected and washed with anhydrous benzene. To the sodium derivative of p-anisoyl hydroxymethylene ketone obtained was added 35 ml of ethylene glycol and then 75 ml of glycol containing 12 g of hydrogen chloride was introduced dropwise. The mixture obtained was stirred for 1.5 hours and then left overnight. The mineral precipitate was then removed by filtration and the filtrate diluted with water and extracted five times with benzene. The benzene extracts were dried over magnesium sulfate, the solvent removed and the residual oil extracted many times with boiling ligroine. We obtained 3.7 g (10.4%) of the ethylene acetal of p-anisoylacetaldehyde with m.p. 65-66°.

Reduction of ethylene acetal of benzoylacetaldehyde with lithium aluminum hydride. With stirring, a solution of 25.4 g of the ethylene acetal of benzoylacetaldehyde in 250 ml of absolute ether was added dropwise to an ether solution of 2.53 g of lithium aluminum hydride with the ether boiling gently and the mixture was stirred and left overnight. The alcoholate formed was decomposed with dilute hydrochloric acid and the ether layer separated and dried over magnesium sulfate. Distillation yielded 21 g (82%) of the ethylene acetal of β-hydroxy-β-phenylpropionaldehyde. After two distillations, the substance was obtained as a thick, colorless liquid without smell; it was miscible with organic solvents, insoluble in water and did not change on storage.

B.p. 128-129° (2 mm), $n^{20}D$ 1.5310, d^{20}_4 1.1487.

Found %: C 69.34, 69.27; H 7.30, 7.28. $C_{11}H_{14}O_3$. Calculated %: C 68.01; H 7.26.

Interaction of ethylene acetal of β-hydroxy-β-phenylpropionaldehyde with polyphosphoric acid. With stirring and cooling, 20 g of polyphosphoric acid was added portionwise to 13.5 g of the ethylene acetal of β-hydroxy-β-phenylpropionaldehyde and the mixture stirred for 10 minutes and then treated with water. The usual processing yielded cinnamaldehyde with b.p. 93-94° (3 mm), $n^{20}D$ 1.6140.

The semicarbazone (m.p. 207°) did not depress the melting point of an authentic sample of cinnamaldehyde semicarbazone.

According to data in [13]: b.p. 112° (8 mm), $n^{20}D$ 1.6195; according to data in [14]: m.p. of semicarbazone 208°.

SUMMARY

1. A general method was developed for synthesizing the ethylene acetals of β-keto aldehydes of the aromatic series by interaction of aryl β-chlorovinyl ketones with ethylene glycols in the presence of alkaline agents.

2. Interconversions between alkoxyvinyl ketones, dialkyl acetals, and ethylene acetals were accomplished in the presence of alkaline agents.

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SYNTHETIC INVESTIGATIONS IN THE FIELD OF POLYENE COMPOUNDS

XV. TOTAL SYNTHESIS OF CITRAL

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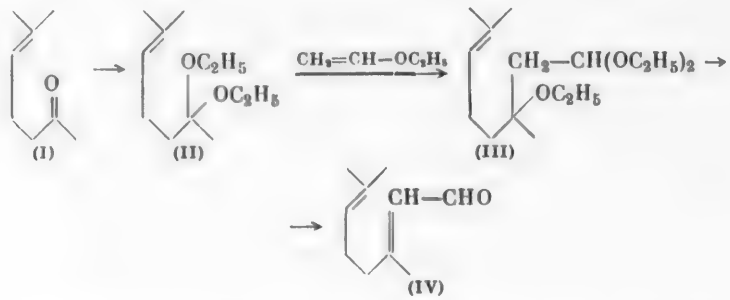
L. T. Zhikhareva, V. I. Koltunova, and N. A. Preobrazhenskii

All-Union Scientific Research Institute of Vitamins

Citral is the starting material for the synthesis of vitamin A, carotinoids and a series of aromatic principles. The synthesis we developed for 6-methylhepten-5-one-2 (I) from acetone and acetylene [1, 2] by the pyrolysis of acetoacetic esters of tertiary ethylene carbinols [3] makes it advantageous to use this substance for the synthesis of citral.

The conversion of methylheptenone to citral has been achieved by condensation with ethoxyacetylenylmagnesium bromide, partial hydrogenation and hydrolysis of the 1-ethoxy-3,7-dimethyloctadien-2,6-ol-3 formed [4] and later by the condensation of methylheptenone with acetylene, partial hydrogenation, conversion of the linalool formed to geranyl bromide and interaction of the latter with 2-nitropropane in an alkaline medium [5].

We were able to prepare citral from methylheptenone without the use of organometallic synthesis by the following scheme.



The diethyl ketal of 6-methylhepten-5-one-2 (II) was prepared in 95-97% yield by the use of the readily available tetraethoxysilane in the presence of orthophosphoric acid [6], a small amount of p-toluenesulfonic acid and about 0.3 mole of alcohol to 1 mole of starting ketone.

We studied the interaction of ketal (II) with ethyl vinyl ether under the action of catalytic amounts of boron trifluoride etherate and anhydrous zinc chloride. It was found that in contrast to boron trifluoride, the use of a solution of zinc chloride in glacial acetic acid led to the formation of a considerably lesser amount of high-boiling, side condensation products and made it possible to obtain 3,7-dimethyl-1,1,3-triethoxyoctene-6 (III) in 60-65% yield.

The subsequent reaction, hydrolysis of the acetal and elimination of a molecule of alcohol, proceeded with a citral yield of 42-45% under the action of a 15% solution of sodium acetate in acetic acid [7] for 30 minutes at a temperature of 108-110°. With a more prolonged reaction, self-condensation of the citral

occurred, as we showed in a control experiment. The citral content of the reaction product after distillation was determined polarographically. Pure citral was obtained from the reaction mixture by isolation of its bisulfite derivative.

The semicarbazone obtained from citral had m.p. 132.5-136°, from which it follows that during the elimination of the molecule of alcohol, two geometrically isomeric forms of the aldehyde were formed [8].

EXPERIMENTAL

1. Diethyl ketal of 6-methylhepten-5-one-2 (II). 60.0 g of 6-methylhepten-5-one-2 (I) ($n^{20}D$ 1.4400) was dissolved in 179.25 g of tetraethoxysilane and 4.57 g of orthophosphoric acid and 0.0015 g of p-toluenesulfonic acid in 6.6 ml of ethanol added. The reaction mixture was left at room temperature for 4-5 days. 500 ml of an 8% methanol solution of sodium hydroxide was added. The mixture was heated at 40-50° under reflux for 1 hour. It was then cooled to room temperature, poured into 1500 ml of water with vigorous stirring and extracted with ether. The combined extracts were washed with water and dried with potassium carbonate. The solvent was evaporated and the residue distilled. The yield was 92.5 g (97.3%).

B.p. 42-44° (2 mm), $n^{20}D$ 1.4350, d^{20}_4 0.8618, MR_D 60.58; calc. 60.435.
Found %: C 71.71, 71.75; H 11.51, 11.87. $C_{12}H_{24}O_2$. Calculated %: C 72.00; H 12.00.

2. 3,7-Dimethyl-1,1,3-triethoxyoctene-6 (III). With stirring in an atmosphere of nitrogen, to 53 g of the diethyl ketal of 6-methylhepten-5-one-2 (II) was added 2.78 ml of a 10% solution of fused zinc chloride in glacial acetic acid (0.5% of zinc chloride to the weight of ketal), containing 0.0027 g of p-toluenesulfonic acid. 25.2 ml of ethyl vinyl ether (b.p. 35-35.6°) was added dropwise to the reaction mixture over a period of 1 hour with stirring at 30° and stirring was continued at 30-35° for a further 1 hour. The mixture was cooled to room temperature, poured into 80 ml of water and extracted with ether. The combined extracts were washed with saturated sodium bicarbonate solution and dried with potassium carbonate. The solvent was removed and the residue distilled. The 1st fraction had b.p. 75-88° (7 mm), $n^{20}D$ 1.434, 31.0 g; 2nd fraction b.p. 106-110° (0.2 mm), $n^{20}D$ 1.4455, 16.53 g; 3rd fraction b.p. 115-138° (0.2 mm), $n^{20}D$ 1.4562, 4.05 g.

The 1st fraction was reacted diethyl ketal of 6-methylhepten-5-one-2 (58.5% of that taken for reaction).

The 2nd fraction was the condensation product (60% yield on the ketal of methylheptenone reacting).

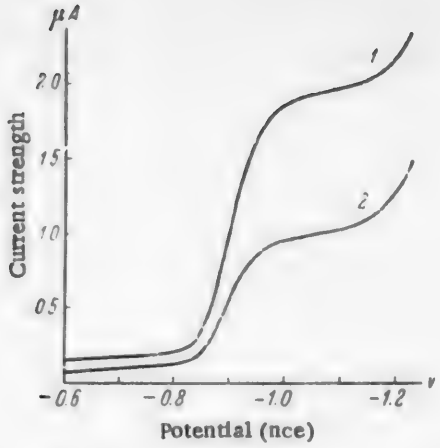
$n^{20}D$ 1.4455, d^{20}_4 0.9053, MR_D 80.13; calc. 80.55.
Found %: C 70.94; H 11.59. $C_{16}H_{32}O_3$. Calculated %: C 70.58; H 11.76.

The 3rd fraction was the product of further condensation with the vinyl ether.

3. Citral. A warm solution of 16.4 g of anhydrous sodium acetate in 100 ml of glacial acetic acid and 12 ml of water, containing 5-10 mg of hydroquinone, was added with stirring to 27.2 g of 3,7-dimethyl-1,1,3-triethoxyoctene-6 (III). The reaction mixture was heated for 30 minutes at 108-110°, cooled, poured into 500 ml of water, neutralized with sodium bicarbonate and extracted with ether. The ether solutions were washed with water and dried with magnesium sulfate. Removal of the solvent and distillation yielded 12.6 g of a substance with b.p. 57-106° at 3 mm. According to a polarographic determination, the citral content of this substance was 50.6%. The citral yield was 41.5%. The citral content was determined on an electronic polarograph of the PÉ-312 type. The capillary constants were t 0.28 sec and m 0.35 mg/sec. The polarogram of pure citral on a base electrolyte of 0.5 N HCl in a 50% ethanol medium had $E_{1/2}$ −0.90 v (Figure, curve 1) relative to a normal calomel electrode [9]. *

A sample of 100 g of the substance investigated was transferred to a 25 ml measuring flask with 96% alcohol. A 2 ml sample was taken and dissolved in 8 ml of alcohol and 10 ml of 0.5 N hydrochloric acid. The solution obtained was placed in a polarographic cell and thermostatted while a stream of nitrogen was passed and a polarogram plotted, beginning at −0.6 v. The current strength was 0.825 μamp (Figure, curve 2).

* The authors would like to thank V. A. Devyatnin for making it possible to carry out the polarographic investigation.



Samples of polarograms. 1) Citral, 2) crude reaction product.

Semicarbazone. When a warm solution of 0.34 g of crude citral in 0.64 ml of ethanol was added to a mixture of 0.28 g of semicarbazide hydrochloride with 0.237 g of potassium acetate in 0.46 ml of ethanol, crystals were deposited. The 0.2 g of semicarbazone was collected and recrystallized from 0.4 ml of ethanol. We obtained citral semicarbazone with m.p. 132.5-136°. The yield was 0.18 g (77%).

Found %: N 20.19, 19.90. $C_{11}H_{19}ON_3$. Calculated %: N 20.09.

Purification of citral. Into a mixture of 23.5 ml of water, 23.5 g of crushed ice, 11.0 g of anhydrous sodium sulfite, and 7.5 g of sodium bicarbonate was introduced 12.6 g of crude citral. The mixture was stirred vigorously at room temperature for 5 hours. The impurities that did not react were extracted from the solution obtained with ether. The aqueous layer was returned to the reaction flask, 10 ml of ether added, the mixture stirred vigorously for 10 minutes, 18.4 ml of a 10% aqueous solution of sodium hydroxide slowly added dropwise and the mixture shaken for 5-7 minutes and transferred to a separating funnel. The layers were separated and the aqueous one further extracted with ether. To the aqueous layer was again added 5 ml of ether and 5 ml of a 10% aqueous solution of sodium hydroxide, the mixture stirred vigorously and allowed to settle, the layers separated and the aqueous one further extracted with ether. The combined extracts were dried with magnesium sulfate, the solvent removed and the residue distilled. The yield of citral was 6.2 g (49.1%). The b.p. was 55-56° (1 mm), $n^{20}D$ 1.4891.

Found %: C 78.65, 78.71; H 10.81, 10.61. $C_{10}H_{16}O$. Calculated %: C 78.96; H 10.53.

SUMMARY

The total synthesis of citral was achieved on the basis of the previously synthesized 6-methylhepten-5-one-2, which was condensed as its diethyl ketal with ethyl vinyl ether and the 3,7-dimethyl-1,1,3-triethoxy-octene-6 formed was subsequently hydrolyzed with the simultaneous elimination of alcohol.

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ACYLPYRAZOLES

II. SYNTHESIS AND ACIDITY CONSTANTS OF 3-AROYLPYRAZOLES

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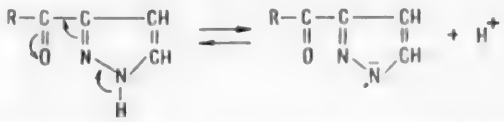
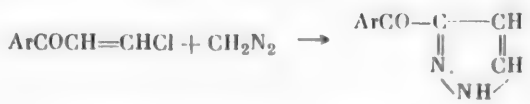
Moscow State University

In a previous article [1] we presented data on the acid properties of some 3-acylpyrazoles and discussed the problem of the nature of these acid properties. The latter may be considered as due to a tautomeric shift of the multiple bonds with the formation of an O-metallic derivative, as was proposed by A. N. Nesmeyanov and one of us [2], or it can be considered that the hydrogen of the ring nitrogen shows acid properties due to the presence of a negative substituent in the nucleus. Despite the fact that previously we showed a preference for the first possibility [1], we later established unequivocally [3] by an investigation of the infrared spectra of 3-acylpyrazoles and their salts that salt formation was not connected with a tautomeric shift of bonds in the 3-acylpyrazole system and we can only consider the appearance of acid properties of the ring hydrogen atom.



The spectrophotometric method of determining the acidity constants of 3-acylpyrazoles, which we used previously [1], made it possible to evaluate quantitatively the acidity in relation to the nature of the acyl radical. Until now the acidity of not only pyrazole derivatives, but of nitrogen-containing heterocycles in general has hardly been investigated quantitatively. On the example of the acidity of various acyl derivatives of pyrazole, we undertook a study of this problem, which is interesting from a theoretical point of view. In the present work, we present data on the acidity constants of 3-aroylpyrazoles (I), containing substituents in the nucleus, which made it possible to evaluate the effect of the character of the carbonyl group of the 3-acylpyrazole on the acid properties of the latter.

Since 3-benzoylpyrazole [2, 4] was the only 3-aroylpyrazole known previously, we synthesized analogs of this compound containing a methyl, methoxyl or a nitro group and a chlorine atom in the para-position of the phenyl nucleus. The synthesis was carried out by the method developed previously for 3-acylpyrazoles, namely interaction of appropriate aryl β-chlorovinyl ketones [5, 6] with diazomethane in an ether solution [2].



(I)

Ar = p-$CH_3C_6H_4$, p-$CH_3OC_6H_4$, p-ClC_6H_4, p-$O_2NC_6H_4$.

The reaction proceeded quite smoothly and the yield of 3-aroylpyrazoles was 40-80%. Thus, the method of synthesizing 3-acylpyrazoles proposed previously [2] has a quite general character. The 3-aroylpyrazoles obtained were stable, readily crystallizable substances, which dissolved in aqueous solutions of alkalis and were recovered by acidification.

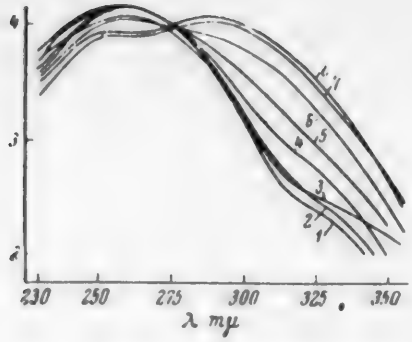


Fig. 1. Ultraviolet absorption spectra of 3-benzoylpyrazole. 1) in 1 N HCl; pH value: 2) 7, 3) 10, 4) 11, 5) 11.5, 6) 12, 7) 13, 8) 14.

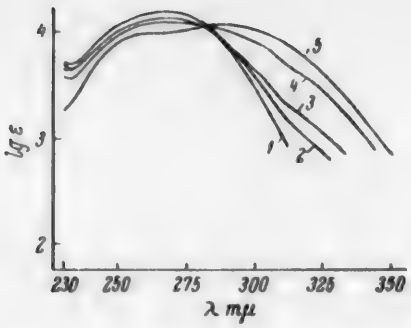


Fig. 2. Ultraviolet absorption spectra of 3-p-chlorobenzoylpyrazole. pH value: 1) 10, 2) 11, 3) 11.5, 4) 12, 5) 14.

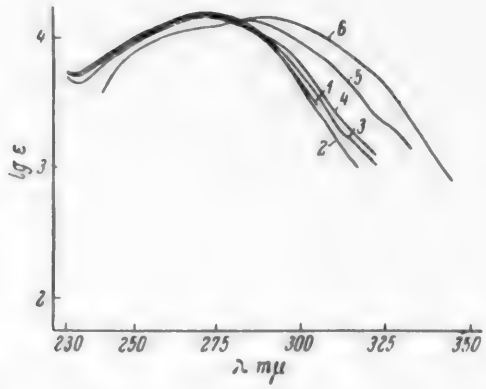


Fig. 3. Ultraviolet absorption spectra of 3-p-tolylpyrazole. pH values: 1) 7, 2) 10, 3) 11, 4) 11.5, 5) 12, 6) 14.

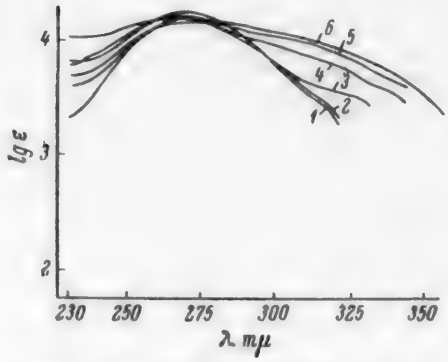


Fig. 4. Ultraviolet absorption spectra of 3-p-nitrobenzoylpyrazole. pH value: 1) 7, 2) 11, 3) 11.5, 4) 12, 5) 12.5, 11.5, 6) 14.

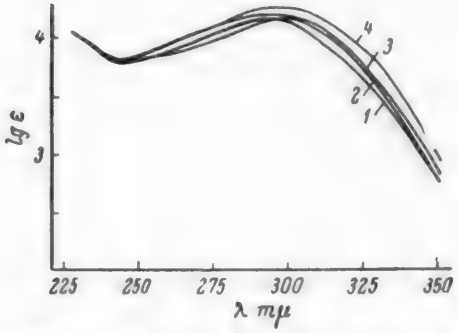


Fig. 5. Ultraviolet absorption spectra of 3-p-methoxybenzoylpyrazole. pH value: 1) 7, 2) 11.5, 3) 12, 4) 14.

To determine the acidity constants of these substances, we used the spectrophotometric method [1, 7, 8] and plotted the ultraviolet absorption spectra in aqueous buffer solutions with various pH values (from 7 to 14). The spectra of 3-p-chlorobenzoylpyrazole and 3-p-tolylpyrazole were very similar to each other and also to the previously described [1] spectrum of 3-benzoylpyrazole. In a neutral medium, the spectrum consisted of two bands: an intense shortwave band and a low-intensity longwave band, marked only by two points of inflection [in the case of 3-p-chlorobenzoylpyrazole and 3-p-tolylpyrazole, only the beginning of the longwave band is seen in the spectra presented (Figs. 2 and 3) since, due to the poor solubility of these compounds in water, only the part of the spectrum in the region of strong absorption could be obtained clearly]. In an alkaline medium the main absorption maximum was shifted by 20-30 mμ toward longer wavelengths and in the place of the previous maximum of the shortwave band, a horizontal or very slightly sloping section of the spectral curve remained. The spectral curves of 3-p-chlorobenzoylpyrazole and 3-p-tolylpyrazole had a clear isosbestic point, indicating the presence of an acid–base equilibrium.

The spectra of 3-p-nitrobenzoylpyrazole and 3-p-methoxybenzoylpyrazole (Figs. 4 and 5) showed only one broad absorption band both in neutral and in an alkaline medium and the position of the maximum was not shifted in going from one medium to the other. Nonetheless, in the case of the first of the compounds named, there was a considerable difference between the spectra plotted in different media; in the case of the second, this difference was only slight. Evidently, the difference of these spectra from those of the other aroylpyrazoles investigated was caused by the presence of the strongly chromophoric groups (NO_2 and CH_3O) in the para-position of the phenyl ring.

The acid dissociation constant was calculated by the method of Stenström and Goldsmith [7]:

$$k = a_H \frac{\epsilon - \epsilon_{AH}}{\epsilon_A - \epsilon}$$

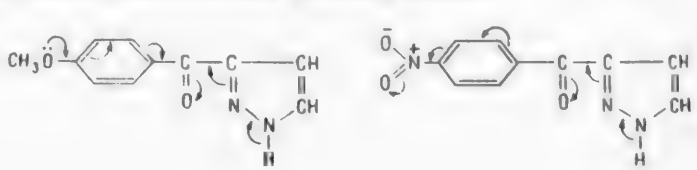
K is the acid dissociation constant, AH, the activity of protons in the given solution, ϵ, the molar absorption coefficient of the solution of the given pH, ϵ_{AH}, the molar absorption coefficient of the undissociated molecule and ϵ_A, the molar absorption coefficient of the aroylpyrazole anion.

As in previously described cases [1], we assume that $pH = -\log a_H$ and also that $\epsilon_A - = \epsilon$ at pH 14. The values of K were calculated by the method of least squares (cf. [8]) from the experimental values of ϵ, obtained at different wavelengths. The results obtained agreed well with each other. This method was found to be unsuitable only in the case of 3-p-methoxybenzoylpyrazole, since here the spectral curves at different pH values differed too little from each other and the error in the calculations was too great. We therefore used a graphical method to obtain the acidity constant of 3-p-methoxybenzoylpyrazole [7] and employed the spectrophotometric titration curves at several wavelengths. An example of such a curve is given in Fig. 6. In all cases, we took as the constant the average value obtained from calculations at different wavelengths.

TABLE 1

Substance	λ_{max} (in mμ)		λ of isosbestic point	pK
	neutral medium	alkaline medium		
3-p-Methoxybenzoylpyrazole	296	296	—	12.09
3-p-Tolylpyrazole	272	287	282	12.02
3-Benzoylpyrazole	260	291	275	11.97
3-p-Chlorobenzoylpyrazole	268	288	283	11.87
3-p-Nitrobenzoylpyrazole	272	272	—	11.68

The basic data of the spectrophotometric investigation and the calculated acidity constants for the 3-aroylpyrazoles synthesized are presented in Table 1; data for 3-benzoylpyrazole, which were taken from a previous communication [1], are also included for comparison. The data in the table show that the acidity constants of the 3-aroylpyrazoles investigated change quite sharply in relation to the nature of the substituent in the para-position of the phenyl nucleus. Electron-donor substituents (CH_3- and especially CH_3O-groups) lower the acidity constant, while electron-acceptors (Cl and NO_2-groups), on the contrary, raise the acidity in comparison with unsubstituted benzoylpyrazole. This effect is explained by the fact that electron-donor substituents, which donate electrons through the aromatic system of the benzene ring, partially neutralize the effect of the carbonyl group on the pyrazole ring. The action of electron-acceptor groups is directly opposite:



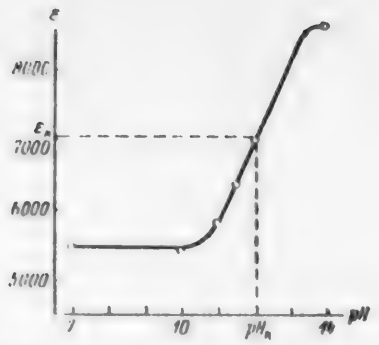


Fig. 6. Spectrophotometric titration curve. 3-p-Methoxybenzoylpyrazole at 31,000 cm^{-1}.

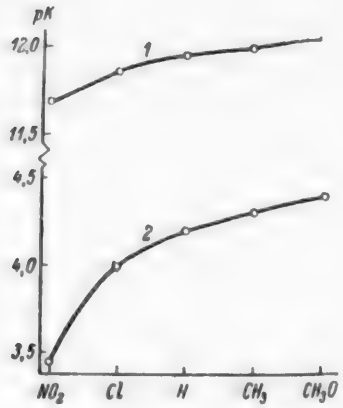


Fig. 7. Effect of substituents in the para-position of the phenyl nucleus on the acidity of 3-aroylpyrazoles (1) and benzoic acids (2).

The data in the table also shows that the acidity of 3-aroylpyrazoles in relation to the substituent in the phenyl nucleus falls in the series $O_2N > Cl > H > CH_3 > CH_3O$, which agree completely with the series of acidity constants of analogously substituted benzoic acids [9, 10]. As is seen from Fig. 7, in the case of aroylpyrazoles this effect is weaker as in this case, the effect of the substituent on the N–H bond is also transmitted through the aromatic system of the pyrazole ring and is distributed between two equivalent nitrogen atoms. The data obtained make it possible to arrive at an important conclusion: the acidity of nitrogen-containing heterocyclic systems, determined by the ease of dissociation of an N–H bond, obeys the same rules which control the dissociation of normal carboxylic acids.

EXPERIMENTAL

p-Tolyl β-chlorovinyl ketone, p-chlorophenyl β-chlorovinyl ketone, p-nitrophenyl β-chlorovinyl ketone [5] and p-methoxyphenyl β-chlorovinyl ketone [6] were obtained by known methods.

3-Aroylpyrazoles. To a dried solution of diazomethane, obtained from 10.5 g of nitrosomethylurea in 120 ml of ether, was added 0.05 mole of aryl-β-chlorovinyl ketone in 50 ml of absolute ether in small portions. The solution was rapidly decolorized and deposited colorless crystals of the hydrochloride of the corresponding 3-aroylpyrazole. The crystals were collected and treated with a warm 15% solution of sodium carbonate until the evolution of carbon dioxide ceased. The precipitate of aroylpyrazole was collected, dried and recrystallized. Data on the 3-aroylpyrazoles obtained by this method are presented in Table 2.

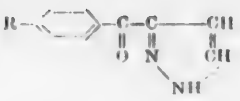
Solutions. Standard phosphate (pH 7-8) and glycine (pH 9-13) buffer solutions were used as solvents in the spectrophotometric measurements. 1 N sodium hydroxide solution was used as a buffer solution with pH 14. Samples of the substances investigated were weighed out on a microbalance and dissolved in definite volumes of solvent (due to the very low solubility of the aroylpyrazoles, it was often necessary to use prolonged shaking). Where necessary, the initial solutions were diluted to the required concentration with appropriate buffer solutions.

Spectra. The optical density of the solutions was measured on the spectrovisor system of Dianov-Klokov [11, 12], fitted to the optical system of an SF-4 spectrophotometer.* Cells with quartz windows 0.5 cm thick were used. We did not check that aroylpyrazoles obeyed the Lambert-Beer law since they are chemically similar to acetylpyrazoles, which were investigated previously and which strictly obey this law [1]. Also, in plotting the spectra and changing from one concentration to another, we did not observe deviations from the Lambert-Beer law.

The spectral curves obtained are presented in Figs. 2-5. The previously described spectra of 3-benzoylpyrazole (Fig. 1) are also presented for comparison (Fig. 1).

*We are very grateful to I. V. Obreimov for making it possible to work on a Dianov-Klokov spectrovisor system and for valuable advice.

TABLE 2

3-Aroylpyrazoles Obtained 

R	Yield (in %)	Melting point	% C		% H		% N	
			found	calc.	found	calc.	found	calc.
CH_3O	80	97—97.5° (from water)	65.33, 65.21	65.38	5.23, 5.04	4.98	14.05, 13.75	13.86
CH_3	75	134.5—135 (from benzene)	71.17, 71.13	70.94	5.73, 5.68	5.41	15.00, 15.10	15.06
Cl	41	129—131 (from benzene)	58.29, 58.17	58.12	3.70, 3.52	3.42	13.59, 13.75	13.56
NO_2	56	187—187.5 (from nitro-benzene)	55.38, 55.20	55.29	3.73, 3.45	3.25	19.56, 19.31	19.35

SUMMARY

1. Interaction of aryl β-chlorovinyl ketones with diazomethane yielded 3-aroylpyrazoles containing substituents in the aromatic nucleus (40-80% yields).

2. The ultraviolet absorption spectra of 3-aroylpyrazoles at various pH values of the medium were plotted and the acid dissociation constants calculated from the data obtained. It was shown that the acidity of 3-aroylpyrazoles depends on the substituent in the phenyl nucleus and falls in the series $O_2N > Cl > H > CH_3 > CH_3O$, which completely corresponds to the effect of these substituents on the dissociation constant of the corresponding para-substituted benzoic acids.

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SYNTHESIS AND CATALYTIC CONVERSIONS OF 2-METHYLBICYCLO-(2,2,2)-OCTANE AND 2,3-DIMETHYLBICYCLO-(2,2,2)-OCTANE

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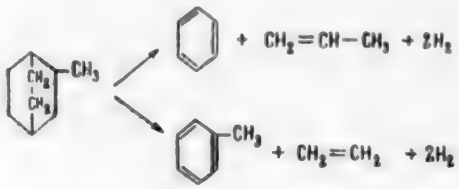
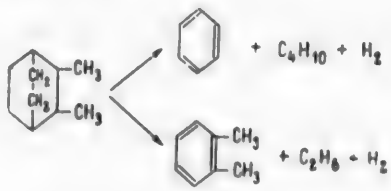
It was previously shown [1] that in the presence of platinized charcoal at 300-310°, 2-methylbicyclo-(2,2,2)-octane was converted into toluene with a small amount of benzene.



For a more detailed investigation of this reaction, we synthesized again 2-methylbicyclo-(2,2,2)-octane and the previously undescribed 2,3-dimethylbicyclo-(2,2,2)-octane and carried out the catalytic conversions of these hydrocarbons under the conditions indicated above.

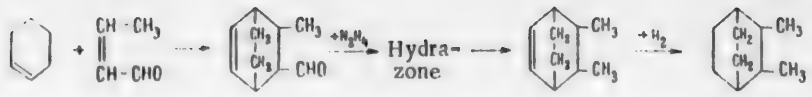
It was found that they behaved differently: 2-methylbicyclo-(2,2,2)-octane was almost completely converted into aromatic hydrocarbons with a considerable predominance of toluene (benzene was only detected as traces); under analogous conditions, 2,3-dimethylbicyclo-(2,2,2)-octane was only 30% converted into a mixture of benzene (about 1/3) and o-xylene (about 2/3).



The gaseous hydrocarbons formed from 2-methylbicyclooctane and 2,3-dimethylbicyclooctane had a saturated character.

EXPERIMENTAL

1. The synthesis of the hydrocarbons was achieved by the interaction of cyclohexadiene-1,3 with acrolein or crotonaldehyde and subsequent conversion of the resulting bicyclic aldehydes by the Kizhner method.



Cyclohexadiene-1,3- was synthesized by a slightly modified procedure [2]. To a gently boiling solution of sodium alcoholate, prepared from 1500 ml of 96% alcohol and 120 g of sodium, was added 486 g of dibromocyclohexane. After being boiled for 6-8 hours on a water bath, the mixture was cooled with snow and salt, the solution carefully decanted and the sodium bromide precipitate rapidly collected on a Buchner funnel and dissolved in a small amount of water; the upper layer was separated and the lower one extracted with ether. The alcohol solution and filtrate were mixed and distilled from a Favorskii flask; fractions were obtained: 1st 60-70° (mixture of alcohol and cyclohexadiene), 2nd 70-78° (alcohol with some diene), 3rd 78° (alcohol),and 4th above 78° (alcohol and 1-ethoxycyclohexene-2).

The second fraction was redistilled; its low-boiling part was added to the 1st fraction and the residue, to the 3rd. The 1st fraction was washed with a concentrated solution of calcium chloride, dried with calcium chloride and distilled over metallic sodium in a stream of nitrogen or carbon dioxide. The yield of cyclohexadiene with b.p. 79-80° was 32-40 g (20-22%).

The 4th fraction was washed with water and calcium chloride solution; the wash waters were extractedwith ether. To the 1-ethoxycyclohexene-2 isolated from the 4th fraction was added the 1-ethoxycyclohexene-2 isolated by solution of the sodium bromide precipitate. The dried product was distilled first without sodium and then boiled for 1 hour with sodium and distilled over it. The yield was 144-150 g (57-59%).

B.p. 153-154° (755 mm), $n^{20}D$ 1.4524, d^{20}_4 0.8952, MR_D 38.01. $C_8H_{14}O$ F_1. Calculated 38.12.

1-Ethoxycyclohexene-2 was converted into cyclohexadiene-1,3 by distillation with freshly prepared potassium bisulfate. 10 g of potassium bisulfate and 10 g of 1-ethoxycyclohexene-2 were placed in a 100 ml Claisen flask, which was heated to 150-160° on an oil bath. As the cyclohexadiene formed distilled, a further 190 g of ethoxycyclohexene was gradually introduced into the flask at the same temperature. The temperature of the emergent vapor did not exceed 80°. The diene was washed free from alcohol with calcium chloride solution, dried,and distilled. The yield was 105-115 g (85-90%).

B.p. 79.5-80° (747 mm), $n^{20}D$ 1.4750, d^{20}_4 0.8406, MR_D 26.77. C_6H_8 F_2. Calculated 26.77.

For the preparation of 2-methylbicyclo-(2,2,2)-octane, 40 g of cyclohexadiene-1,3 and 28 g of acrolein in a sealed ampoule were heated at 100° for 8 hours. Distillation of the reaction product yielded 2-methylalbicyclo-(2,2,2)-octene-5 with b.p. 84-85° (12 mm) (55 g; 80.8%). The aldehyde was purified through the semicarbazone (m.p. 177-178°).

B.p. 84-85° (12 mm), $n^{20}D$ 1.4995, d^{20}_4 1.0346, MR_D 38.68. $C_9H_{12}O$ F_1. Calculated 38.91.

From 136.2 g of the aldehyde we obtained 92 g (75%) of 2-methylbicyclo-(2,2,2)-octene-5 by Kizhner's method.

B.p. 148-149° (750 mm), $n^{20}D$ 1.4767, d^{20}_4 0.8939, MR_D 38.61. C_9H_{14} F_1. Calculated 38.90

62 g of unsaturated hydrocarbon, 30 ml of alcohol,and 4 g of Raney nickel were placed in a hydrogenation flask , into which hydrogen was introduced with shaking until the calculated volume had been absorbed. The saturated hydrocarbon formed precipitated from the solution as solid balls, which were collected and dissolved in a small amount of n-pentane; the solution was washed with water, dried with calcium chloride, treated with a small amount of Katvinkel's mixture, washed again, dried, and pentane removed and the 2-methylbicyclo-(2,2,2)-octane distilled over metallic sodium. The yield was 60 g (92%).

B.p. 158-158.5° (749 mm), m.p. 33-34°, $n^{40.5}D$ 1.4608, $d^{40.5}_4$ 0.8664, MR_D 39.33. C_9H_{16}. Calculated 39.36.

2,3-Dimethylbicyclo-(2,2,2)-octane was synthesized from 100 g of cyclohexadiene-1,3 and 90 g of crotonaldehyde. After being heated in a sealed ampoule for 22 hours at 180-190°, the mixture was distilled. Fractions were obtained: 1st 78-160°, 68 g; 2nd 85-89° (10 mm), 115 g; 3rd 90-92° (10-12 mm), 5 g.

The 1st fraction was heated for a further 10 hours at 180-190°; it yielded a further 30 g of aldehyde. After purification through the semicarbazone (m.p. 173-174°), the aldehyde (a total of 145 g; 70%) had:

B.p. 88-90° (12 mm), 83-85° (8 mm), $n^{20}D$ 1.4945, d^{20}_4 0.9953, MR_D 43.17. $C_{10}H_{14}F_1$. Calculated 43.52. Found %: C 79.31, 79.35; H 9.22, 9.32. $C_{10}H_{14}O$. Calculated %: C 79.96; H 9.38.

60 g of the aldehyde was dissolved in 25 ml of anhydrous alcohol and 22.2 g of hydrazine hydrate in 25 ml of anhydrous alcohol added dropwise to the solution. The mixture was heated for 14 hours under reflux at 75-78° (thermometer in liquid). The alcohol was removed on an oil bath and the hydrazone dried with lumps of potassium hydroxide. Without distillation, the hydrazone was decomposed by Kizhner's method by dropwise addition to 12 g of solid potassium hydroxide and a lump of platinized charcoal in a Claisen flask with a distillation condenser. The oil bath temperature was 170-180°. The hydrocarbon distillate was washed with 10% hydrochloric acid and water, dried with calcium chloride, and distilled with metallic sodium.

B.p. 160-162° (753.5 mm), $n^{20}D$ 1.4715, d^{20}_4 0.8820, MR_D 43.21. $C_{10}H_{16}F_1$. Calculated 43.51. Found %: C 87.88, 88.18; H 12.03, 12.00. $C_{10}H_{16}$. Calculated %: C 88.18; H 11.82.

40 g of the unsaturated hydrocarbon was hydrogenated in alcohol in the presence of Raney nickel. We isolated 40 g of hydrocarbon.

B.p. 173-174° (750 mm), $n^{20}D$ 1.4620, d^{20}_4 0.8744, MR_D 43.86. $C_{10}H_{18}$. Calculated 43.98. Found %: C 87.05, 86.98; H 13.28, 13.08. $C_{10}H_{18}$. Calculated %: C 86.98; H 13.02.

2. Catalytic conversions of 2-methylbicyclo-(2,2,2)-octane and 2,3-dimethylbicyclo-(2,2,2)-octane.

Fifteen g (50 cc) of platinized charcoal (15% platinum), prepared according to data in [3], was placed in a glass tube, which was inserted into a tubular furnace with a thermoregulator. The hydrocarbon was introduced dropwise from an automatic burette or a dropping funnel; the catalyzate was collected in snow and salt cooled receiver, connected to a spiral trap in a Dewar vessel with a mixture of dry ice and acetone. A temperature of 300° and a volume rate of cyclohexane throughput of 0.5-0.98 $hours^{-1}$ gave a product with $n^{20}D$ 1.4958, i.e., the catalyst was quite active.

37.2 g of 2-methylbicyclo-(2,2,2)-octane was run from a heated funnel into the tube with a volume rate of 0.2 $hours^{-1}$ at 300-305°. After 3 passes through the catalyst, the reaction product had $n^{20}D$ 1.4863. The gas emerging from the tube contained 57% of H_2 and 42% of C_2H_6. 20 g (28 ml) of catalyzate was distilled on a column of 43 theoretical plates (Table 1).

TABLE 1

Fraction No.	Boiling point at 760 mm	Content (in vol. %)	n_D^{20}	Comments
1	108.47—110.57°	3.5	1.4970	
2	110.57	64.3	1.4965	
3	110.62—158.12	8.0	1.4728	
4	158.12	4.3		
Residue		9.9		Crystals with m.p. 33—34°

In Experiment 2, 24.8 g of 2-methylbicyclo-(2,2,2)-octane was passed through the catalyst 6 times at the same temperature and a volume rate of 0.25 $hours^{-1}$. We obtained 12.8 of catalyzate with $n^{20}D$ 1.4958 and b.p. 90-115°, consisting almost solely of toluene with a small amount of benzene. The gas consisted of 55% H_2 and 45% C_2H_6. Oxidation with potassium permanganate by Ullmann's method yielded benzoic acid with m.p. 121.5°.

TABLE 2

Fraction No.	Boiling point at 760 mm	Content (in vol. %)	n_D^{20}	d_4^{20}	Solidification point
1	79.7°	11.0	1.5000	0.8790	+ 5.5°
2	82.6—138.1	6.2	1.4912	—	—20
3	138.1—142.2	9.8	1.4985	0.8650	—23.9
4	142.2—143.9	5.4	1.5000	0.8660	—25
5	144.2—152.2	2.1	1.4740	—	—
Residue		44.5		—	—

2,3-Dimethylbicyclo-(2,2,2)-octane was converted under the same conditions with the same catalyst and in the same apparatus: after 4 contacts 27.6 g of hydrocarbon gave 24 g of product with $n^{20}D$ 1.4768, which was distilled on a column of 43 theoretical plates (Table 2).

The 1st fraction was almost pure benzene. After distillation from a Favorskii flask, the residue was found to be almost unchanged 2,3-dimethylbicyclo-(2,2,2)-octane. Fractions 2-4 were oxidized by Ullmann's method; only phthalic acid with m.p. 231° was obtained in all cases, indicating the presence of o-xylene.

As a special experiment showed, the catalyst retained its initial activity with respect to cyclohexane.

SUMMARY

1. 2,3-Dimethylbicyclo-(2,2,2)-octane was synthesized for the first time.

2. 2-Methylbicyclo-(2,2,2)-octane was almost wholly converted into toluene in the presence of platinized charcoal at 300°.

3. Under the same conditions, 2,3-dimethylbicyclo-(2,2,2)-octane was 30% converted into a mixture of benzene (1/3) and o-xylene (2/3).

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1,4-ENDOETHYLENE-5,6,7,8-TETRAHYDRONAPHTHALENE

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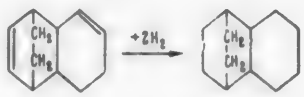
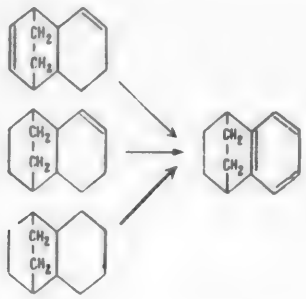
It was previously shown [1] that at 240-250° in the presence of platinized charcoal the dimer of cyclohexadiene-1,3 (endoethylenehexahydronaphthalene) and its dihydro derivative (endoethyleneoctahydronaphthalene) were converted into a crystalline hydrocarbon with m.p. 63-64° with the evolution of hydrogen.

In the present work it was shown that the tetrahydro derivative of the dimer (endoethylenedecahydronaphthalene), described by Alekseevskii [2], was readily obtained by the equation

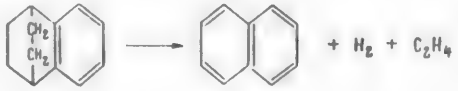


by hydrogenation of the dimer under pressure at normal temperature; under the conditions indicated above this compound was also smoothly converted into the same hydrocarbon with m.p. 63-64°.

Thus, under catalytic dehydrogenation conditions, all the endoethylenehydronaphthalenes were capable of the conversions:



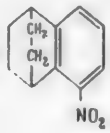
The structure of the hydrocarbon thus obtained (m.p. 63-64°), which did not have normal double bonds, was not proved by direct experiments, strictly speaking, though it follows from the reaction equations presented. It was quite stable in the presence of platinized charcoal at 250 and 315-320°. As Kazanskii and Vol'fson [1] reported, a certain amount of naphthalene was formed at 350°, but this could not be isolated. The formation of naphthalene indicated that the reaction proceeded by the equation:



This direction is characteristic of different hydrocarbons of the bicyclo-(2,2,2)-octane-3,4 series, which are converted into aromatic hydrocarbons under catalytic dehydrogenation conditions with the liberation of one of the bicyclooctane "bridges" [3].

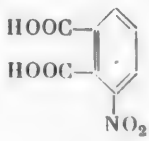
In the present work, on one hand, we attempted to achieve a smooth conversion of endoethylenetetrahydronaphthalene and endoethylenedecahydronaphthalene into naphthalene. It was found that they were almost completely converted into naphthalene at 400°, which is an argument in favor of the structure proposed for the hydrocarbon with m.p. 63-64°. Naphthalene homologs, whose possible formation was considered in the article of Alekseevskii [2], were not detected.

On the other hand, we showed that the molecule of endoethylenetetrahydronaphthalene contained an aromatic nucleus by obtaining a series of substitution products, characteristic of aromatic compounds. It was found, for example, that the action of a nitrating mixture formed a mononitro derivative with a nitro group in position 5.

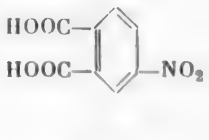


It was reduced to an amine of aromatic character, which was capable of being diazotized and gave an aromatic diazo compound; coupling the latter with dimethylaniline, β-naphthol, and H-acid yielded corresponding azo dyes.

The structure of the nitro compound was proved by its oxidation to 3-nitrophthalic acid (I).



(I)



(II)

We could not detect the formation of 4-nitrophthalic acid (II), which could be obtained simultaneously with (I) by oxidation of the tetralin nitro derivative.

Evidently the sulfonyl group entered the same position during sulfonation with dioxane–sulfur trioxide; the sulfonic acid could readily be converted into a sulfonyl chloride and the latter into a sulfamide by reactions characteristic of aromatic compounds. Bromination of the hydrocarbon yielded a monobromide of aromatic character.

Thus, the experiments in this work showed that the hydrocarbon with m.p. 63-64° was 1,4-endoethylene-5, 6,7,8-tetrahydronaphthalene, as was proposed by Kazanskii and Vol'fson.

EXPERIMENTAL

Synthesis of starting hydrocarbons. 1. Dimer of cyclohexadiene-1,3 (1,4-endoethylenehexahydronaphthalene). 220 g of cyclohexadiene-1,3 [4] was heated in an autoclave for 25 hours at 180-190°. Distillation of the reaction product yielded fractions: 1st b.p. 80-85° (760 mm), 104 g (47%); 2nd b.p. 110-111° (14 mm), 110 g (50%); 3rd b.p. above 111° (14 mm), 4.5 g (2%).

The 1st fraction (cyclohexadiene-1,3) was again dimerized (yield of dimer 50%). A total of 200 g of dimer was obtained:

B.p. 110-111° (14 mm), $n^{20}D$ 1.5269, d^{20}_4 0.9960, MR_D 49.44. $C_{12}H_{16}F_2$. Calculated 50.08.

2. 1,4-Endoethyleneoctahydronaphthalene. 50 g of 1,4-endoethylenehexahydronaphthalene was hydrogenated in the presence of Raney nickel in alcohol solution at normal pressure. After the addition of 1 mole of hydrogen, the absorption rate fell sharply and hydrogenation was discontinued.

B.p. 101-102° (8 mm), $n^{20}D$ 1.5090, d^{20}_4 0.9561, MR_D 50.67. $C_{12}H_{18}F_1$. Calculated 50.55.

3. 1,4-Endoethylenedecahydronaphthalene. 50 g of 1,4-endoethylenehexahydronaphthalene was hydrogenated in the presence of 6 g of Raney nickel at room temperature in an autoclave at an initial hydrogen pressure of 140 atm. Hydrogen absorption was complete after 5-6 minutes. The catalyst was removed by filtration

and the hydrocarbon obtained was treated with monohydrate to remove possible residual unsaturated compounds. The hydrogenated product did not react with monohydrate in the cold.

B.p. 104° (9 mm), $n^{20}D$ 1.5070, d^{20}_4 0.9621, MR_D 50.82; calc. 51.01.
Found %: C 87.86, 86.92; H 12.26, 12.23. $C_{12}H_{20}$. Calculated %: C 87.74; H 12.26.

Catalytic conversions of hydrocarbons in the presence of platinized charcoal. All three hydrocarbons were passed in succession at 250° in a stream of CO_2 with a volume rate of 0.24 $hours^{-1}$ through a tube with platinized charcoal (15% platinum). In all cases the same crystalline hydrocarbon, 1,4-endoethylenetetrahydronaphthalene, was formed in 80-95% yield and after recrystallization from alcohol, it had m.p. 63.5°. The gases liberated during the reaction contained only hydrogen in addition to carbon dioxide.

At 400° and with a volume rate of 0.3 $hours^{-1}$ in the presence of the same catalyst, 1,4-endoethylenetetrahydronaphthalene was converted into naphthalene, which melted at 80° after recrystallization from alcohol and sublimation. A mixture with pure naphthalene melted at the same temperature.

1,4-Endoethylenedecahydronaphthalene was also converted into naphthalene under the same conditions.

Derivatives of 1,4-endoethylenetetrahydronaphthalene. 1) 5-Nitro-1,4-endoethylenetetrahydronaphthalene. 15.8 g of finely powdered 1,4-endoethylenetetrahydronaphthalene was nitrated at −5° with a mixture of 7.2 ml of HNO_3 (d 1.4) and 13 ml of H_2SO_4 (d 1.84). The liquid reaction mass was again placed in a cooling mixture and the precipitate collected, washed with warm (60-70°) water and recrystallized from hot methyl alcohol. The nitro compound formed yellowish, needle-like crystals with m.p. 68.5-69°.

Found %: N 7.13, 6.93. $C_{12}H_{13}O_2N$. Calculated %: N 6.99.

For establishing the position of the nitro group, 5 g of nitroendoethylenetetrahydronaphthalene was oxidized with a solution of chromic acid in glacial acetic acid according to data in [5]. The crystals of 3-nitrophthalic acid obtained melted at 212-213° (in a sealed capillary). A mixture with 3-nitrophthalic acid, which has m.p. 218°, melted at 211-212°. 4-Nitrophthalic acid melts at 161-163°.

2. 5-Amino-1,4-endoethylenetetrahydronaphthalene. 20.32 g of nitroendoethylenetetrahydronaphthalene was reduced with 35 g of metallic tin and 80 ml of hydrochloric acid (d 1.19). After being heated on a water bath, the mixture was diluted with water and a solution of 45 g of sodium hydroxide in 60 ml of water added to it to a strongly alkaline reaction. The amine was steam distilled; after drying in a vacuum desiccator, the crystals melted at 57-58°.

Found %: N 8.19, 8.33. $C_{12}H_{15}N$. Calculated %: N 8.09.

Aminoendoethylenetetrahydronaphthalene hydrochloride was diazotized with sodium nitrite solution in the cold. The diazo compound was coupled with dimethylaniline (brown crystals), with β-naphthol (sodium salt — red crystals) and with H-acid (dark violet crystals).

3. Endoethylenetetrahydronaphthalenesulfonic acid. Endoethylenetetrahydronaphthalene did not react with sulfuric acid (d 1.84) at room temperature. A crystalline sulfonic acid was obtained at 60-70° and this gave a barium salt with an aqueous suspension of barium hydroxide.

Found %: Ba 22.44, 22.45. $(C_{12}H_{13}SO_3)_2Ba$. Calculated %: Ba 22.40.

The sulfonation was carried out more conveniently with dioxane–sulfur trioxide. With stirring, 2.01 g of dioxane – sulfur trioxide in 2.5 ml of dichloroethane was added to a cooled solution of 1.58 g of endoethylenetetrahydronaphthalene in dichloroethane (2-3 ml). The sulfonic acid was isolated as the barium salt or as the compound with dioxane, which reacted readily with phosphorus pentachloride to form endoethylenetetrahydronaphthalenesulfonyl chloride with m.p. 107.5-108.5° and reaction of the latter with ammonia yielded the sulfonamide.

4. Endoethylenetetrahydronaphthalene monobromide. 1.58 g of endoethylenetetrahydronaphthalene was mixed with 3 g of dioxane dibromide [6]. After 1-2 minutes, voluminous evolution of hydrogen bromide began and the mixture changed to a liquid mass. The reaction was complete after 1 hour; its product, a heavy oil, was extracted with ether, washed with sodium carbonate solution and dried with calcium chloride; the ether was removed and the bromide vacuum distilled.

B.p. 150-152° (10 mm), $n^{20}D$ 1.5871, d^{20}_4 1.3810, MR_D 57.55. $C_{12}H_{13}Br$ F_3. Calculated 57.38.

Found %: C 60.80, 60.79; H 5.47, 5.54. $C_{12}H_{13}Br$. Calculated %: C 60.78; H 5.52.

SUMMARY

1. Endoethylenehexahydronaphthalene, endoethyleneoctahydronaphthalene, and endoethylenedecahydronaphthalene are converted into endoethylenetetrahydronaphthalene in the presence of platinum at 250°.

2. Endoethylenetetrahydronaphthalene and endoethylenedecahydronaphthalene are converted into naphthalene at 400° with the same catalyst.

3. The structure of endoethylenetetrahydronaphthalene is confirmed by the nitro, amino, sulfonic acid, and bromo derivatives, which are described in the present work.

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INTERACTION OF TETRAHYDROSYLVAN WITH SILICON TETRACHLORIDE

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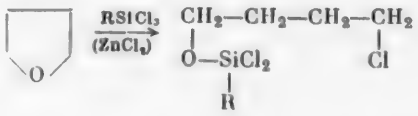
Under the action of compounds containing an active halogen atom, the tetrahydrofuran ring may be cleaved in two ways.

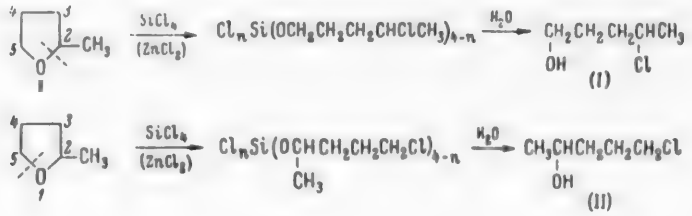
1) Hydrogen halides [1], aluminum chloride and bromide [2], phosphorus tribromide, titanium tetrachloride, antimony pentachloride [3], phosgene [4], and alkyldichlorosilanes [5] cleave the tetrahydrofuran ring at both C—O bonds to form 1,4-dihaloalkanes.

2) Silicon tetrachloride [6] and alkyl- and aryltrichlorosilanes [5] in the presence of zinc chloride as catalyst open the tetrahydrofuran ring predominantly at one C—O bond with the chlorine atom adding to the carbon atom and the free valences of the oxygen and silicon atoms forming a new bond.

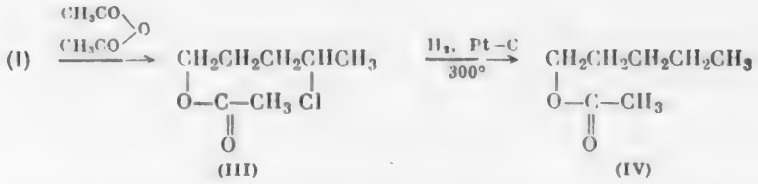


In the general case, ring cleavage of α-substituted tetrahydrofuran homologs may lead to two products due to the asymmetry of the molecule. Thus, for example, it was established [7] that the interaction of tetrahydrosylvan with acetyl chloride produced ring cleavage at C—O bond adjacent to the methyl group. However, if the reaction was carried out in the presence of hydrogen chloride, the other C—O bond, which was not adjacent to the methyl substituent, was cleaved. Morell [8] found that under the action of acetyl bromide the tetrahydrosylvan ring was cleaved in both possible directions and the ratio of the isomers formed depended on the reaction temperature: an increase in the latter favored rupture of the C—O bond, distant from the side group.

In the present work, we investigated the reaction of tetrahydrosylvan with silicon tetrachloride. This reaction proceeds only in the presence of anhydrous zinc chloride. When vacuum distilled, the reaction products underwent intensive decomposition and therefore they were decomposed with water and then the hydrolysis products distilled on a column at reduced pressure. This yielded 1,4-dichloropentane (15-20%) and a chlorine substituted amyl alcohol (70-80%), which could have been obtained as a result of hydrolysis of a chloroester of silicic acid.



Depending on which C—O bond, 1-2 or 1-5, was cleaved, an alcohol with a primary (I) or secondary (II) hydroxyl group (4-chloropentanol-1 or 5-chloropentanol-2) could have been formed. The structure of the chlorohydrin formed by hydrolysis was proved by the following conversions:



5-Chloropentanol-2 should have given sec-amyl acetate as a result of these conversions. Reductive dehalogenation of 2-chloro-5-acetoxypentane (III) on platinized charcoal in the vapor phase proceeded very smoothly with high yields (95%) of primary amyl acetate (IV). Thus, the chlorohydrin formed by hydrolysis of the reaction products of tetrahydrosylvan and silicon tetrachloride was 4-chloropentanol-1, i.e., under the action of silicon tetrachloride, the ring in tetrahydrosylvan was cleaved at the C—O bond adjacent to the methyl group.

EXPERIMENTAL

Tetrahydrosylvan was obtained by hydrogenation of sylvan in an autoclave over a skeletal nickel-aluminum catalyst at 100-120°; b.p. 79-80° (750 mm), $n^{20}D$ 1.4058, and d^{20}_4 0.8582. When distilled with a fractionating column, the silicon tetrachloride boiled over the range 58-60°.

Tetrahydrosylvan was reacted with silicon tetrachloride according to the following procedure. Into a flask fitted with a reflux condenser was placed 2 moles of tetrahydrosylvan, 2 moles of silicon tetrachloride and 1 g of anhydrous zinc chloride. The reaction mixture was boiled for 14 hours and then, after distillation of the unreacted silicon tetrachloride, it was decomposed with water. The hydrolysis products were extracted several times with ether, washed with sodium carbonate solution, dried with potassium carbonate and after evaporation of the ether, distilled in a column with glass packing at reduced pressure. Fractions were isolated: 1st b.p. 57-58° (7 mm), $n^{20}D$ 1.4486, d^{20}_4 1.0739 — 1,4-dichloropentane (15-20% yield); 2nd b.p. 76-77° (9 mm), $n^{20}D$ 1.4503; d^{20}_4 1.0393; found MR_D 31.72. $C_8H_{11}OCl$. Calculated 31.68. Yield 70-80%.

The 2nd fraction, 4-chloropentanol-1, for which the literature [9] gives only b.p. 78-80° (10 mm), was acetylated with acetic anhydride with cooling.

Chloropentanol acetate had b.p. 112-113° (11 mm), $n^{20}D$ 1.4336, d^{20}_4 1.0194.

Reductive dehalogenation of the chloropentanol acetate was carried out by a flow method in the vapor phase on platinized charcoal at 290-300° and normal pressure. The 5% platinized charcoal was prepared by impregnating activated charcoal with the calculated amount of chloroplatinic acid solution and reducing with hydrogen at 250-300°. After one pass of the acetate at a volume rate of 0.1 $hours^{-1}$, the catalyzate had $n^{20}D$ 1.4012. It was then treated with sodium carbonate solution until the evolution of carbon dioxide ceased and separated from the aqueous layer, which was extracted 2-3 times with ether and the ether extract combined with the bulk of the material and dried with sodium sulfate.

The reduction products were distilled on a column with a glass packing. We isolated unreacted 2-chloro-5-acetoxypentane and primary amyl acetate (90-95%):

B.p. 146.5-148° (741 mm), $n^{20}D$ 1.4015, d^{20}_4 0.8781. Literature data [10]: b.p. 148°, d^{20}_{20} 0.879.

SUMMARY

1. It was shown that when reacted with silicon tetrachloride in the presence of zinc chloride, the tetrahydrofuran ring with an alkyl substituent in the α-position was opened at the C—O bond adjacent to the side alkyl group.

2. It was found that 2-chloro-5-acetoxypentane smoothly underwent reductive dehalogenation in the vapor phase over Pt—C at 300° to form m-amyl acetate.

3. The reaction of tetrahydrosylvan with silicon tetrachloride may serve as a convenient method of preparing 4-chloropentanol-1.

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TETRAACYLOXYSILANES IN ORGANIC SYNTHESIS

XXIII. ACYLATION OF AMINES, ARYLHYDRAZINES, AND ACID HYDRAZIDES WITH TETRAACYLOXYSILANES

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In previous work [1], a description was given in the acylation of diethylamine with tetracycloxysilanes as a convenient method of preparing N,N-diethylamides of saturated, monobasic organic acids (60-90% yields).

$$(RCOO)_4Si + 4NHR'R'' \rightarrow 4RCONR'R'' + Si(OH)_4$$

In connection with this it seemed worthwhile extending this method to the preparation of other N,N-dialkylamides and also acid N-alkylamides and determining its applicability to the synthesis of N,N-diethylamides of aromatic acids – benzoic and o- and p-toluic, which are repellents [2, 3].

We acylated dibutylamine with the silicoanhydrides of acetic, propionic, butyric, and caproic acids and obtained the N,N-dibutylacylamides of these acids in yields of 65-81%.

By acylating diethylamine with the silicoanhydrides of benzoic and o- and p-toluic acids, we obtained N,N-diethylbenzamide (63%), N,N-diethyl-o-toluamide (24%) and N,N-diethyl-p-toluamide (37%), respectively. The low yields of the diethylamides of the toluic acids in comparison with the yields of dialkylamides of aliphatic acids [1] were caused by the greater strength of these aromatic acids and especially of o-toluic acid. On the example of the acylation of benzene and thiophene, we established previously that the acylating capacity of a tetraacyloxysilane fell with an increase in the strength of the acid forming it [4].

Friedel and Ladenburg [5], who first described silicoacetic anhydride, reported that when ammonia was passed into its benzene solution, acetamide was formed. By passing ammonia and ethylamine into a benzene solution of silicoacetic anhydride, we obtained acetamide and N-ethylacetamide in yields of only 12% and 5-6%, respectively. On acylating ethylamine by heating with tetraacyloxysilanes in an autoclave at 100°, we obtained the N-ethylamides of acetic, propionic, butyric, valeric, isovaleric, and caproic acids in yields of 33-82%.

As regards the acylation of phenylhydrazine, according to literature data the following have been used for this: acid anhydrides (yields up to 83%) [6-8], esters (10-82%) [9-11], vinyl acetate (74-98%) [12] and acids themselves [13-17]. Acetic anhydride was used for the acylation of acetylhydrazine [18]. In the present work we acylated phenylhydrazine with the silicoanhydrides of acetic and propionic acids and obtained the phenylhydrazides of these acids, N-acetyl- and N-propionyl-N'-phenylhydrazine, in yields of 67% and 61%, respectively.

$$4C_6H_5NHNH_2 + (RCOO)_4Si \rightarrow 4C_6H_5NHNHCOR + Si(OH)_4$$

Acylation of acetylhydrazine with silicoacetic anhydride led to the formation of N,N'-diacetylhydrazine in 85% yield.

$$4CH_3CONHNH_2 + (CH_3COO)_4Si \rightarrow 4CH_3CONHNHCOCH_3 + Si(OH)_4$$

Substituted Amides and Hydrazides of Acids Obtained by Acylation of Amines and Substituted Hydrazines with Tetraacyloxysilanes

Name	Yield (in %)	Temperature: melting point	Temperature: b.p. (pressure in mm)	n_D^{20}	d_4^{20}	MR_D: found	MR_D: calc.*	Literature data
N,N-Dibutylacetamide	81.0	—	109—110°(8)	1.4469	0.8772	52.17	52.00	B. p. 126—131° (17 mm), n_D^{20} 1.4427 [20]
N,N-Dibutylpropionamide	65.0	—	115—116 (7)	1.4472	0.8778	56.43	56.62	B.p. 122° (10mm), n_D^{20} 1.4469, d_4^{20} 0.8758 [21]
N,N-Dibutylbutyramide	75.0	—	123—124 (7)	1.4483	0.8718	61.24	61.24	B. p. 155—155.5° (30mm), n_D^{20} 1.4485, d_4^{20} 0.8707 [19]
N,N-Dibutylcaproamide	70.0	—	146—147 (7)	1.4508	0.8656	70.71	70.47	B.p. 130° (2mm) [22]
N,N-Diethylbenzamide**	63.0	—	129 (5)	1.5257	1.016	53.51	53.02	B. p. 173—175° (35mm) [23], d_4^{20} 1.010 [24]
N,N-Diethyl-o-toluamide	24.0	49—50°	143 (6)	—	—	—	—	M.p. 49—50°, B.p. 105° (1mm) [2]
N,N-Diethyl-p-toluamide	37.0	53.5—55.8	130—130.5 (3)	—	—	—	—	M. p. 53.5—55.5°, B.p. 110° (1mm) [2]
N-Ethylacetamide	33.0	—	87—89 (7)	1.4338	0.9237	24.54	24.53	B.p. 109.5—110.5° (22 mm), n_D^{20} 1.4338, d_4^{20} 0.9237 [19]
N-Ethylpropionamide	60.0	—	94—95 (7)	1.4365	0.9110	28.98	29.15	B.p. 94—95° (7 mm) [25]
N-Ethylbutyramide***	82.0	—	101—102 (7)	1.4372	0.9028	33.42	33.77	
N-Ethylvaleramide****	64.0	—	113—115 (7)	1.4405	0.8910	38.25	38.39	
N-Ethylisovaleramide	70.0	35—37	104—105 (7)		—	—	—	M.p. 20—30°, B.p. 121° (20 mm) [26]; M.p. 68°, B.p. 105—107° (14mm) [27]
N-Ethylcaproamide	74.5	—	126—127 (7)	1.4445	0.8826	43.13	43.00	B.p. 152—154° (14mm) [26]
N-Acetyl-N'-phenylhydrazine	67.0	128—129.5	—	—	—	—	—	M.p. 129° [7]
N-Propionyl-N'-phenylhydrazine	61.0	157—158	—	—	—	—	—	M.p. 157—158° [29]
N,N'-Diacetylhydrazine	85.0	139.5—140	—	—	—	—	—	M.p. 140° [18]

*In calculating the additive values of MR_D for N,N-dialkyl- and N-ethylamides, we took the atomic refraction of nitrogen as 2.508 and 2.750, respectively; values determined by B. V. Ioffe [19].

**Found %: N 7.64, 7.67, 8.15. $C_{11}H_{15}ON$. Calculated %: N 7.90.

***Found %: C 62.49, 62.53; H 11.26, 11.30; N 11.86, 11.94. $C_6H_{13}ON$. Calculated %: C 62.56; H 11.38; N 12.16.

****Found %: C 64.81, 64.69; H 11.82, 11.76; N 10.88, 10.89. $C_7H_{15}ON$. Calculated %: C 65.06; H 11.70; N 10.89. Not described in the literature.

EXPERIMENTAL

Preparation of N,N-dialkylamides of acids. Into a three-necked flask, fitted with a stirrer, a reflux condenser with a calcium chloride tube and a gas inlet tube leading to the bottom of the flask, was placed 100 ml of dry benzene, 0.1 mole of monobasic acid and 0.03 moles of silicon tetrachloride and the mixture heated for 5-6 hours so that a steady evolution of hydrogen chloride occurred. When the evolution of hydrogen chloride ceased, for its complete removal and that of the residual silicon tetrachloride, a stream of dry air was passed through the solution of silicoanhydride for 30 minutes. The flask was cooled with ice water, the gas inlet tube replaced by a dropping funnel and 0.07 mole of secondary amine (0.2 mole in the case of silicoanhydrides of aromatic acids) added dropwise with stirring; afterward the mixture was heated for 5-6 hours on a water bath at 60-70° and then for a further 1 hour with the water bath boiling. The reaction mixture was cooled and the silicic acid precipitate removed by filtration and washed with benzene. In the preparation of the isomeric o- and p-diethyltoluamides, the benzene solution was washed with a 10% solution of sodium hydroxide and in the preparation of the dibutylamides of aliphatic acids, with minimal amounts of 5% hydrochloric acid, water, 5% sodium hydroxide solution and water. The solution was dried with anhydrous sodium sulfate, the benzene removed and the residue vacuum distilled.

Preparation of N-ethylamides of acids. 50 ml of benzene was distilled from a benzene solution of silicoanhydride obtained from 0.15 mole of organic acid and 0.045 mole of silicon tetrachloride in 100 ml of dry benzene as described above, the solution of silicoanhydride transferred to an autoclave cooled with ice and salt and 0.25 mole of strongly cooled ethylamine added. The autoclave was closed and heated with constant shaking for 5-6 hours at 100°. The autoclave was cooled and opened and the silicic acid filtered from the solution and washed with acetone. To remove traces of acid, the benzene–acetone solution of the amide was left to stand or shaken with baked potassium carbonate (until the evolution of carbon dioxide ceased). After removal of the solvent, the reaction product was vacuum distilled.

Preparation of phenyl- and acetylhydrazides of acids. To a benzene solution of silicoanhydride obtained from 0.1 mole of acid and 0.03 mole of silicon tetrachloride in 50 ml of dry benzene, as described above, a solution of 0.1 mole of phenylhydrazine in 30 ml of benzene was added dropwise or 0.1 mole of acetylhydrazine was introduced and the mixture heated for 5 hours on a boiling water bath. After cooling, the precipitate of silicic acid and the corresponding hydrazide was collected by filtration and the latter dissolved by washing the precipitate with hot alcohol on the filter. After removal of the alcohol, the hydrazide was recrystallized from alcohol.

The substituted amides and hydrazides of acids obtained by these procedures are listed in the table.

SUMMARY

The acylation of primary and secondary amines and aryl- and acylhydrazines by tetraacyloxysilanes may serve as a method of synthesizing substituted amides and aryl- and acylhydrazides of acids, respectively.

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CHEMISTRY OF SELENOPHENE

XIX. 2-ACETOSELENOPHENE IN THE SYNTHESIS OF α- AND β-KETOALDEHYDES OF THE SELENOPHENE SERIES

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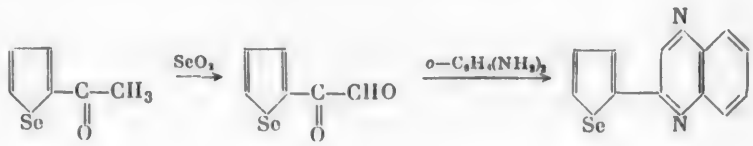
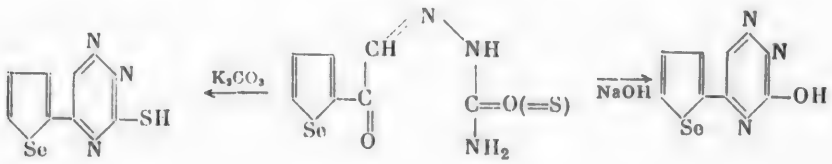
In previous work, one of us [1, 2] described a convenient method of acylation in the selenophene series and the aminomethylation [3] and cyanoethylation [4] of a series of α-acylselenophenes.

In the present work, α-acylselenophenes were used for the synthesis of α- and β-dicarbonyl compounds of the selenophene series. Thus, by oxidation of 2-acetoselenophene with selenium dioxide we obtained selenienyl-2-glyoxal, and α-ketoaldehyde whose bright yellow color is caused by conjugation of the multiple bonds of the two carbonyl groups and the selenophene nucleus. The ultraviolet absorption spectrum of selenienyl-2-glyoxal, presented in Fig. 1, has two maxima at λ 275 and 310 mμ.

Selenienyl-2-glyoxal readily condensed with o-phenylenediamine and quantitatively formed 2-(selenienyl-2'-)quinoxaline.



The monosemicarbazone and monothiosemicarbazone of selenienyl-2-glyoxal lost water when treated with alkalis and cyclized to 3-hydroxy- and 3-mercapto-5-(selenienyl-2')-triazine-1,2,4, respectively.



Condensation of 2-acetoselenophene with ethyl formate under the action of sodium yielded the sodium alcoholate of hydroxymethylene selenienyl-2 ketone (a β-ketoaldehyde derivative), which had a dark violet color, in contrast to analogous compounds of the thiophene series. Its absorption spectrum is presented in Fig. 2, curve I. When treated with copper acetate, this alcoholate readily formed an internal complex of Cu^{++}, whose absorption spectrum is represented by curve II.

Interaction of the alcoholate of hydroxymethylenemethyl selenienyl-2 ketone with methylamine led to the formation of N-methylamino-(selenenoyl)-acetaldehyde.

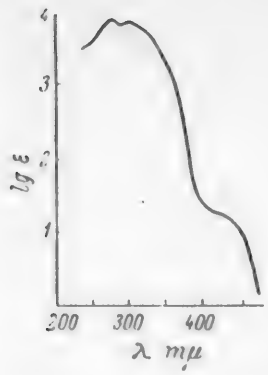


Fig. 1. Ultraviolet absorption spectrum of selenienyl-2-glyoxal.

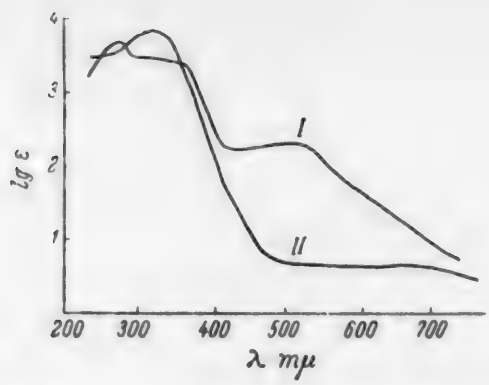
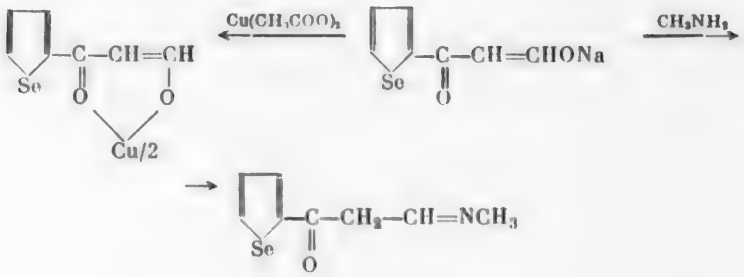


Fig. 2. Ultraviolet absorption spectrum of sodium alcoholate of hydroxymethylene selenienyl-2-ketone. Explanation in text.



EXPERIMENTAL

Selenienyl-2-glyoxal. Into a three-necked flask with a reflux condenser and a stirrer were placed 65 ml of dioxane, 2 ml of water and 11.1 g (0.10 mole) of selenium dioxide and 18 g (0.10 mole) of methyl selenienyl-2 ketone [b.p. 93.5° (7 mm), $n^{20}D$ 1.6011, d^{20}_4 1.5607] was added immediately. The mixture was heated on a boiling water bath for 4 hours, left for 24 hours, and filtered free from selenium. After removal of the dioxane, the reaction product was vacuum distilled. We obtained 14 g (74%) of product:

B.p. 103-104° (8 mm), $n^{20}D$ 1.6280, d^{20}_4 1.6795. MR_D 39.30. $C_6H_4O_2Se$ F_2. Calculated 37.43.
Found %: C 38.73, 38.76; H 2.25, 2.15. $C_6H_4O_2Se$. Calculated %: C 38.52; H 2.17.

Selenienyl-2-glyoxal was a bright yellow, viscous oil; on standing in air, it formed colorless crystals of a hemihydrate, $(C_6H_4O_2Se)_2 \cdot H_2O$, with m.p. 90-91° (from benzene).

Found %: C 36.95, 37.03; H 2.78, 2.83. $C_{12}H_{10}O_5Se_2$. Calculated %: C 36.76; H 2.57.

2-(Selenienyl-2')-quinoxaline. To 2.8 g (0.015 mole) of selenienyl-2-glyoxal was added 1.62 g (0.015 mole) of o-phenylenediamine; the mixture, which evolved heat, crystallized on cooling. We obtained 3.8 g (95%) of a product with m.p. 103-103.5° (from alcohol), which formed colorless, lustrous crystals.

Found %: C 55.82; 55.68; H 3.18, 3.19; N 11.28, 11.39. $C_{12}H_8N_2Se$. Calculated %: C 55.63; H 3.11; N 10.87.

Monosemicarbazone of selenienyl-2-glyoxal. To a solution of 1.2 g (0.01 mole) of semicarbazide hydrochloride and 1.6 g of sodium acetate in 20 ml of 50% alcohol, was added 2 g (0.01 mole) of selenienyl-2-glyoxal and the mixture heated on a boiling water bath. We obtained 2.4 g (92%) of product with m.p. 215-217° (with decomp., from alcohol).

Found %: N 17.47, 17.46. $C_7H_7O_2N_3Se$. Calculated %: N 17.21.

3-Hydroxy-5-(selenienyl-2')-triazine-1,2,4. A mixture of 2.85 g (0.009 mole) of the monosemicarbazone of selenienyl-2-glyoxal and 45 ml of a 20% solution of sodium hydroxide was boiled for 15 minutes; the dirty green crystals formed were dissolved in water (~100 ml) and the hydroxytriazine precipitated by the addition of acetic acid, collected and washed with alcohol. We obtained 2 g (98%) of product with m.p. 264-265° (with decomp. from dioxane), which formed light yellow crystals.

Found %: C 36.78, 36.90; H 2.51, 2.50; Se 34.49, 34.61. $C_7H_5ON_3Se$. Calculated %: C 37.18; H 2.23; Se 34.92.

Monothiosemicarbazone of selenienyl-2-glyoxal. To a solution of 3.0 g (0.015 mole) of selenienyl-2-glyoxal in 5 ml of alcohol was added a solution of 1.9 g (0.015 mole) of thiosemicarbazide hydrochloride in water acidified with acetic acid and the mixture left for 4 hours. We obtained 4.2 g (87.5%) of a product with m.p. 175-176° (with decomp., from methyl alcohol).

Found %: N 17.38, 17.44. $C_7H_7ON_3SSe$. Calculated %: N 17.23.

3-Mercapto-5-(selenienyl-2')-triazine-1,2,4. 3.1 g (0.012 mole) of the monothiosemicarbazone of selenienyl-2-glyoxal was dissolved in an aqueous solution of 2.5 g of potassium carbonate by heating and after decolorization with activated charcoal, the reaction product was precipitated by the addition of 2 N hydrochloric acid. We obtained 2.2 g (75%) of product with m.p. 242-243° (with decomp., from alcohol), which formed light orange crystals.

Found %: C 34.59, 34.52; H 2.35, 2.23; N 18.35, 18.31. $C_7H_5N_3SSe$. Calculated %: C 34.71; H 2.07; N 18.14.

Sodium alcoholate of hydroxymethylenemethyl selenienyl-2 ketone. In a three-necked flask with a dropping funnel, a stirrer and a reflux condenser with a calcium chloride tube a mixture of 16 g (0.085 mole) of methyl selenienyl-2 ketone and 6.8 g (0.090 mole) of ethyl formate was added over a period of 40 minutes to 2.4 g of finely divided sodium in 200 ml of absolute ether. The mixture was stirred for 5 hours and then left for a day, when the dark violet precipitate was collected and washed with absolute ether. We obtained 18 g (95%) of a product with m.p. 315-316° (with decomp.).

Found %: C 37.81, 37.89; H 2.41, 2.44. $C_7H_5O_2SeNa$. Calculated %: C 37.69; H 2.24.

Copper complex of hydroxymethylenemethyl selenienyl-2 ketone. 2.2 g (0.01 mole) of the sodium alcoholate of hydroxymethylenemethyl selenienyl-2 ketone was dissolved in 3 ml of water with heating and the solution filtered, cooled, and poured into 5 ml of a saturated solution of copper acetate. We obtained 1.3 g (56%) of product with m.p. 199-200° (from alcohol), which formed dark green crystals.

Found %: C 36.36, 36.39; H 2.40, 2.58. $C_{14}H_{10}O_4Se_2Cu$. Calculated %: C 36.24; H 2.17.

N-Methylimino-(selenenoyl-2)-acetaldehyde. A mixture of 6.7 g (0.03 mole) of the sodium alcoholate of hydroxymethylenemethyl selenienyl-2 ketone, 2 g (0.03 mole) of methylamine hydrochloride and 2.8 g of anhydrous sodium sulfate was shaken vigorously for 20 minutes, then heated for 40 minutes at 60-70°, cooled and treated with ether 5 times. The ether extracts were dried with anhydrous sodium sulfate and after removal of the ether, the residue recrystallized. We obtained 2.5 g (40%) of a product with m.p. 65.5-66° (from 50% alcohol), which formed straw yellow crystals.

Found %: C 44.63, 44.47; H 4.59, 4.65; N 6.88, 6.78. C_8H_9ONSe. Calculated %: C 44.87; H 4.24; N 6.54.

SUMMARY

1. Oxidation of 2-acetoselenophene with selenium dioxide led to selenienyl-2-glyoxal, which was used for the synthesis of 2-(selenienyl-2')-quinoxaline and also 3-hydroxy- and 3-mercapto-5-(selenienyl-2')-triazines-1,2,4.

2. Condensation of 2-acetoselenophene with ethyl formate in the presence of sodium led to the sodium alcoholate of hydroxymethylenemethyl selenienyl-2 ketone, which formed an internal complex of Cu^{++} (by the action of copper acetate) and N-methylimino-(selenienyl-2)-acetaldehyde (by the action of methylamine).

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*Original Russian pagination. See C. B. Translation.

SYNTHESIS OF HYDROCARBONS

LXX. SYNTHESIS OF DITERTIARY ALKYLMETHANES (C_{14}-C_{17}) WITH THREE QUATERNARY CARBON ATOMS

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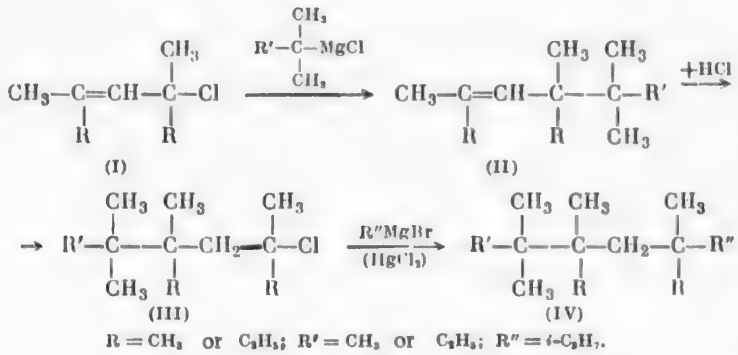
We recently described [1-3] a general method of synthesizing paraffinic hydrocarbons with two quaternary carbon atoms, separated by a methylene group (ditertiary alkylmethanes): tertiary allyl chlorides (I), the monohydrochlorides of 2,4-dimethylpentadiene-1,3 (R = CH_3) or 3,5-dimethylheptadiene-2,4 (R = C_2H_5), were reacted with alkylmagnesium bromides (first Grignard-Wurtz reaction); the alkenes formed were hydrochlorinated and the tertiary saturated chlorides thus obtained were reacted with alkylmagnesium bromides in the presence of mercuric chloride (second Grignard-Wurtz reaction) to synthesize ditertiary alkylmethanes.

In the present work, by using tertiary alkylmagnesium chlorides (instead of the primary or secondary alkylmagnesium bromides we used previously) in the first Grignard-Wurtz reaction, we obtained alkanes (II) with two adjacent quaternary carbon atoms; hydrochlorination of these alkenes yielded the corresponding saturated tertiary chlorides (III) and by a Grignard-Wurtz reaction between these and isopropylmagnesium bromide (in the presence of mercuric chloride) we synthesized ditertiary alkylmethanes (IV) with a highly branched structure, containing three quaternary carbon atoms.

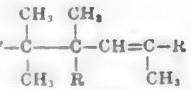


Thus, in the present work we extended the method we developed previously for the synthesis of ditertiary alkylmethanes with two quaternary carbon atoms [1-3] to the synthesis of ditertiary alkylmethanes, containing three quaternary carbon atoms.

EXPERIMENTAL

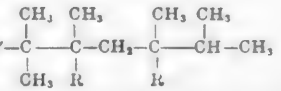
Hydrochlorination of diene hydrocarbons. 2,4-Dimethylpentadiene-1,3 (b.p. 93-94° at 750 mm, $n^{20}D$ 1.4447, d^{20}_4 0.7378; literature data [4]: b.p. 93-94° at 755 mm, $n^{20}D$ 1.4448, d^{20}_4 0.7376) and 3,5-dimethylheptadiene-2,4 (in a mixture with 4-methyl-2-ethylhexadiene-1,3, b.p. 135-141° at 745 mm, $n^{20}D$ 1.4500, d^{20}_4 0.7682; literature

TABLE 1

Alkenes of the General Structure 

R	R′	Name	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	Boiling point (pressure in mm)	Literature data		
							n_D^{20}	d_4^{20}	Literature reference
CH_3	CH_3	2,2,3,3,5-Pentamethylhexene-4	171—172 (760)	1.4459	0.7828	170—170.2 (760)	1.4470	0.7836	[5]
CH_3	C_2H_5	2,4,4,5,5-Pentamethylheptene-2	198—199.5 (755)	1.4592	0.8095	198—199 (750)	1.4589	0.8099	[6]
C_2H_5	CH_3	2,2,3,5-Tetramethyl-3-ethylheptene-4	210—211 (740)	1.4571	0.8015	210.5—211.5 (755)	1.4574	0.8012	[5]
C_2H_5	C_2H_5	3,3,4,6-Tetramethyl-4-ethyloctene-5	96—97 (7)	1.4622	0.8229	97.5—98 (8)	1.4620	0.8226	[6]

TABLE 2

Alkanes of the General Structure 

R	R′	Name	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR_D			Found (%)		Calculated (%)		Yield (in %)
						found	calc.	calc.*	C	H	C	H	
CH_3	CH_3	2,2,3,3,5,5,6-Heptamethylheptane	232—232.2 (739) 95—95.5 (8)	1.4518	0.8102	66.09	66.85	66.03	84.87, 85.04	15.25, 15.12	84.76	15.24	19
CH_3	C_2H_5	2,3,3,5,5,6,6-Heptamethyloctane	111—111.5 (12)	1.4607	0.8268	70.48	71.47	70.42	84.80, 84.99	15.06, 15.11	84.80	15.20	6.5
C_2H_5	CH_3	2,2,3,5,6-Pentamethyl-3,5-diethylheptane	128.5—129 (13)	1.4663	0.8381	74.90	76.09	74.81	84.89, 84.90	15.15, 15.34	84.87	15.13	8
C_2H_5	C_2H_5	2,3,5,6,6-Pentamethyl-3,5-diethyloctane	151—152 (16)	1.4691	0.8464	79.11	80.71	79.20	84.96, 85.05	15.10, 15.11	84.90	15.10	3.5

*$\overline{MR_D}$ calculated by Tatevskii's scheme [7].

data [5]: b.p. 136-142° at 760 mm, $n^{20}D$ 1.4495, d^{20}_4 0.7675) were hydrochlorinated under the conditions described previously [1-3]. During distillation or storage, the monohydrochlorides (I) of these diene hydrocarbons lost hydrogen chloride and therefore they were reacted with tertiary alkylmagnesium chlorides without distillation and directly after their preparation.

Synthesis of alkenes (II). Into a three-necked flask, fitted with a mechanical stirrer, dropping funnel, and reflux condenser, were placed 73 g of magnesium, 300 ml of absolute ether and 2 ml of ethyl bromide. When the reaction began, the stirrer was started and a solution of 3.1 mole of tertiary butyl (R' = CH_3) or tertiary amyl (R' = = C_2H_5) chloride in 1300 ml of absolute ether gradually added at such a rate that the ether dripped only slowly from the reflux condenser (the reaction was carried out without cooling). With the reaction mixture cooled with ice water, an ether solution (1 : 1) of tertiary allyl chloride (I), freshly prepared from 2 moles of diene hydrocarbon, was added dropwise to the tertiary alkylmagnesium chloride prepared. The reaction mixture was stirred for one hour with cooling in the same way and for the same time without cooling, then the next day, it was boiled for 4 hours; the mass was decomposed by pouring onto ice with the addition of acetic acid. The residue obtained after evaporation of the ether from the washed and dried ether extracts was boiled over sodium and distilled. The yields of alkenes (II) were 8-16%, calculated on the allyl chloride (I) introduced into the reaction; their constants are given in Table 1.

The hydrochlorination of the alkenes was carried out by shaking them at room temperature for 3 days with hydrochloric acid, saturated with hydrogen chloride with cooling (ice and salt). The tertiary saturated chlorides (III), which were obtained in 80-90% yield, were separated from the acid, washed only with water, dried with calcium chloride, and reacted with alkylmagnesium bromides without distillation. Their constants were determined after vacuum distillation of a small amount of the substance, but a satisfactory analysis could be obtained only for the first of them, namely, 5-chloro-2,2,3,3,5-pentamethylhexane (R = R' = CH_3; not described in the literature).

B.p. 82-83° (9 mm), $n^{20}D$ 1.4561, d^{20}_4 0.9034, MR_D 57.41; calc. 57.86.
Found %: C 69.26, 69.09; H 12.03, 11.95. $C_{11}H_{23}Cl$. Calculated %: C 69.26; H 12.15.

During storage and distillation, the other tertiary saturated chlorides (III) readily lost hydrogen chloride with the formation of the original alkenes.

Synthesis of ditertiary alkylmethanes (IV) with three quaternary carbon atoms. To isopropylmagnesium bromide (24.3 g of magnesium, 250 ml of absolute ether and 130 g of isopropyl bromide) was added 4 g of mercuric acid chloride and 0.5 mole of tertiary saturated chloride (III) gradually introduced at 12-15°. The next day, the reaction mixture was boiled for 4 hours and decomposed with 2 N hydrochloric acid. After distillation of the ether from the washed and dried ether extract, the residue was boiled for 30 minutes over sodium and vacuum distilled. A fraction of the original alkene (formed by elimination of hydrogen chloride from the tertiary chloride) was collected and also a considerably higher-boiling fraction of ditertiary alkylmethane (IV); the latter was shaken for 1 hour with concentrated sulfuric acid at 60-70° (to decompose traces of organomercury compounds), washed with water, 2 N sodium carbonate solution and again with water, dried with calcium chloride, boiled over sodium, distilled over it in vacuum and fractionated on a column (30 theoretical plates). The ditertiary alkylmethanes (IV) obtained were further purified (after distillation on the column) by chromatography on silica gel. The constants, yields (calculated on the tertiary chloride III introduced into the reaction) and analysis data of the ditertiary alkylmethanes, which were obtained for the first time in the present work, are presented in Table 2.

The data in Table 2 show that the molecular refractions found experimentally differ considerably (up to an order of 1.6 ml/mole) from the values calculated by the usual method (from atomic refractions) and agree well with those calculated by Tatevskii's scheme [7], indicating the need for calculating the molecular refractions of strongly branched hydrocarbons by the more accurate Tatevskii scheme, which takes into account of chemical bond.

The Raman spectra of the ditertiary alkylmethanes synthesized were investigated.* The spectra of all these hydrocarbons contained intense lines in the regions of 670-730, 930- and 1200-1250 cm^{-1}, confirming the presence of quaternary carbon atoms in their molecules [8]. The absence of frequencies in the region of 1600-

*We are grateful to E. G. Treshchova for the optical investigation.

1680 cm^{-1} indicated that the ditertiary alkylmethanes obtained did not contain traces of unsaturated hydrocarbons.

SUMMARY

The general method of synthesizing ditertiary alkylmethanes with two quaternary carbon atoms which we presented previously was extended to the synthesis of ditertiary alkylmethanes containing three quaternary carbon atoms.

By this method we synthesized the previously undescribed ditertiary alkylmethanes with three quaternary carbon atoms: 2,2,3,3,5,5,6-heptamethylheptane, 2,3,3,5,5,6,6 -heptamethyloctane, 2,2,3,5,6 -pentamethyl-3,5-diethylheptane, and 2,3,5,6,6-pentamethyl-3,5-diethyloctane.

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*Original Russian pagination. See C. B. Translation.
**In Russian.

AROMATIC HYDROCARBONS

X. SYNTHESIS OF POLYMETHYLDIETHYLBENZENES FROM ADDUCTS OF 3,4-DIETHYL-2,4-HEXADIENE WITH MALEIC AND ALKYLMALEIC ANHYDRIDES

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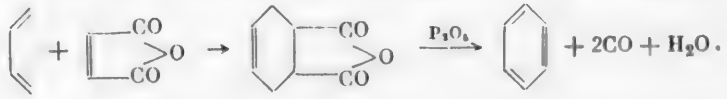
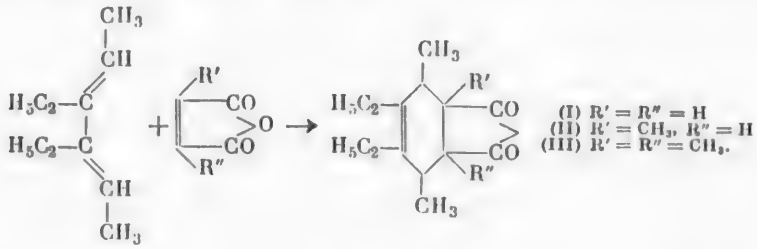
In the preceding communications we described a general method of synthesis of alkylbenzenes with various structures [1-4]. This method consists in the aromatization of tetrahydrophthalic anhydrides (adducts of dienic hydrocarbons with maleic and alkylmaleic anhydrides) under the action of phosphorus pentoxide; the reaction goes with simultaneous detachment of two molecules of carbon monoxide and a molecule of water.



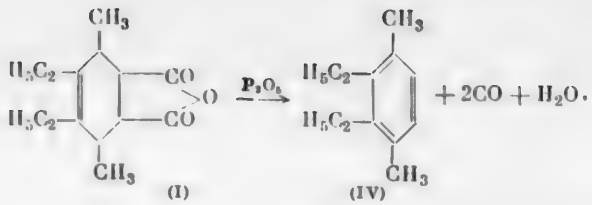
By means of this reaction we obtained high yields of various polymethylbenzenes and some homologs of ethylbenzene free of isomeric alkylbenzenes [2].

In the present work we employed the reaction of aromatization of tetrahydrophthalic anhydrides under the action of phosphorus pentoxide for the preparation of polymethyldiethylbenzenes (dimethyl-, trimethyl- and tetramethyldiethylbenzenes) which had not previously been described in the literature. A study was made of the transformation, under the action of phosphorus pentoxide, of adducts of a tetraalkylbutadiene – 3,4-diethyl-2,4-hexadiene – with maleic, methylmaleic and dimethylmaleic anhydrides.

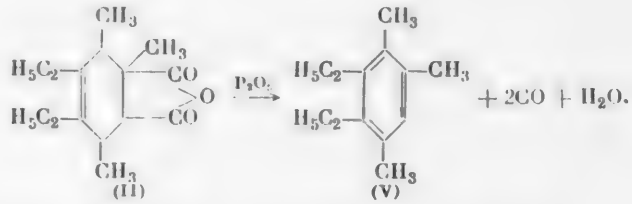
The behavior of 3,4-diethyl-2,4-hexadiene in the diene synthesis has not previously been studied. We prepared adducts of this dienic hydrocarbon with maleic anhydride and its homologs under drastic conditions: heating in an autoclave at 120, 130 and 190° for 10, 20 and 30 hr, respectively (yields 72, 41 and 67% respectively).



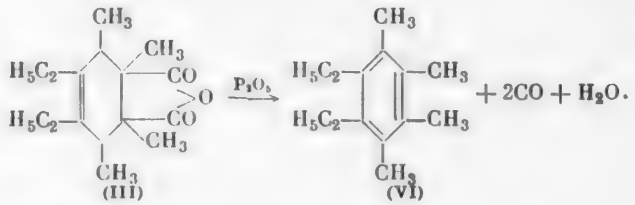
Heating of 3,6-dimethyl-4,5-diethyl-1,2,3,6-tetrahydrophthalic anhydride (I) with phosphorus pentoxide gave 1,4-dimethyl-2,3-diethylbenzene [(IV), yield 71%].



Reaction of phosphorus pentoxide with 2,3,6-trimethyl-4,5-diethyl-1,2,3,6-tetrahydrophthalic anhydride (II) gave 1,2,5-trimethyl-3,4-diethylbenzene [(V), yield 89%].



The adduct of 3,4-diethyl-2,4-hexadiene with dimethylmaleic anhydride – 1,2,3,6-tetramethyl-4,5-diethyl-1,2,3,6-tetrahydrophthalic anhydride (III) – was found to be more resistant to heating with phosphorus pentoxide. 1,2,3,4-Tetramethyl-5,6-diethylbenzene (VI) was obtained (77% yield) only when the reaction mixture was heated 10 hours.



The prepared hydrocarbons, not previously described in the literature, were characterized by their constants; two of them were also characterized by preparation of their sulfonamides.

3,4-Diethyl-2,4-hexadiene, the starting diene for synthesis of polymethyldiethylbenzenes, was obtained in 50-54% yield by dehydration of 3,4-dimethyl-3,4-hexanediol (the pinacone of diethyl ketone) with acetic anhydride in presence of orthophosphoric acid. Since the yield of this pinacone when prepared from diethyl ketone by the usual procedure [5] was only 18%, we evolved a method that enabled its preparation in 40% yield: reduction of diethyl ketone with magnesium amalgam in benzene was effected in presence of a small quantity of methyl iodide which promoted more intensive reduction.

EXPERIMENTAL

Synthesis of 3,4-dimethyl-3,4-hexanediol (pinacone of diethyl ketone). Diethyl ketone (271 g, 3.15 moles) and mercuric chloride (28.5 g, 0.105 mole) were dissolved in anhydrous benzene (300 ml) and the solution was added portionwise to magnesium (36.5 g, 1.52 g-atom). During addition of the first portion of benzene solution of diethyl ketone and mercuric chloride to the magnesium, simultaneous addition was made of 5-8 ml methyl iodide; after the reaction mixture had started to boil vigorously, the remaining solution of diethyl ketone and mercuric chloride was added at such a rate that the benzene continued to boil vigorously. After spontaneous boiling had ceased, the mixture was heated 8 hours, 200 ml anhydrous benzene was then added, and heating was continued for another 8 hours. The reaction mixture was decomposed by heating for 8-10 hours with concentrated ammonium chloride solution. The precipitated magnesium hydroxide was filtered off and washed with benzene. After the benzene had been distilled off from the combined benzene solutions, the 3,4-dimethyl-3,4-hexanediol was distilled in vacuo. Yield 108 g (40%). B.p. 116-119° (7 mm).

Literature: m.p. 27-28° [6]; m.p. 122° (20 mm) [7]; 230° [8].

Synthesis of 3,4-diethyl-2,4-hexadiene. A mixture of the pinacone and acetic anhydride (1:4) was gradually added to a flask (fitted with a column) into which a small quantity of acetic anhydride and a few crystals of orthophosphoric acid had previously been introduced. The hydrocarbon formed in the reaction was distilled in admixture with acetic anhydride at 116-140°; the acetic anhydride was washed out with 2 N sodium carbonate solution; the 3,4-diethyl-2,4-hexadiene was dried with calcium chloride and distilled. Yield 50-54%.

B.p. 154-156° (745 mm), $n^{20}D$ 1.4497.
Literature data [8]: b.p. 153-154°.

Preparation of Adducts of 3,4-Diethyl-2,4-hexadiene

3,6-Dimethyl-4,5-diethyl-1,2,3,6-tetrahydrophthalic anhydride (I) was prepared by heating, in an autoclave for 10 hours at 115-120°, 3,4-diethyl-2,4-hexadiene (11.3 g, 0.082 mole) with maleic anhydride (8.35 g, 0.085 mole) in anhydrous benzene (10 ml). The resulting adduct (13 g, 72%, not described in the literature) was distilled at 193-196° (15 mm), m.p. 88-89° (from ligroine).

Found %: C 71.54, 71.30; H 8.64, 8.69. $C_{14}H_{20}O_3$. Calculated %: C 71.16; H 8.53.

2,3,6-Trimethyl-4,5-diethyl-1,2,3,6-tetrahydrophthalic anhydride (II) was obtained by autoclaving of 3,4-diethyl-2,4-hexadiene (58.5 g, 0.42 mole) with methylmaleic anhydride (47.5 g, 0.42 mole; b.p. 95° at 5 mm [9]) in anhydrous benzene (30 ml) for 15 hours at 128-130°. The adduct (43 g, 41%, not described in the literature) came over at 185-190° (12 mm): m.p. 46-47° (from isopentane).

Found %: C 71.46, 71.46; H 9.07, 9.10. $C_{15}H_{22}O_3$. Calculated %: C 71.96; H 8.81.

1,2,3,6-Tetramethyl-4,5-diethyl-1,2,3,6-tetrahydrophthalic anhydride (III) was obtained by autoclaving 3,4-diethyl-2,4-hexadiene (25 g, 0.18 mole) with dimethylmaleic anhydride (17 g, 0.13 mole, m.p. 96° [10]) 30 hours at 180-190° in presence of a small quantity of hydroquinone and picric acid. The resulting adduct (23 g, 67%, not described in the literature) came over at 200-206° (12 mm): m.p. 58-59° (from ligroine).

Found %: C 72.46, 72.43; H 9.40, 9.37. $C_{16}H_{24}O_3$. Calculated %: C 72.69; H 9.15.

Interaction of the Prepared Polymethyldiethyltetrahydrophthalic Anhydrides with Phosphorus Pentoxide – Preparation of Polymethyldiethylbenzenes

1,4-Dimethyl-2,3-diethylbenzene (IV). A mixture of 3,6-dimethyl-4,5-diethyl-1,2,3,6-tetrahydrophthalic anhydride [(I), 38 g, 0.16 mole] with phosphorus pentoxide (22.7 g, 0.16 mole) was charged into a Wurtz flask (250 ml) equipped with an air condenser. The reaction mixture was gradually heated; after carbon monoxide evolution had ceased, the resulting hydrocarbon was taken off in vacuo, washed with 80% sulfuric acid (for removal of possible traces of original adduct), dried with calcium chloride, and distilled in vacuo. There was obtained 18.6 g (71%) of 1,4-dimethyl-2,3-diethylbenzene (not described in the literature) with the following constants after distillation in a 28-plate column.

B.p. 65.5-66° (4 mm), $n^{20}D$ 1.5105, d^{20}_4 0.8869, MR_D 54.78. $C_{12}H_{18}F_3$. Calculated 54.015, EM_D 0.76.
Found %: C 88.83, C 88.73; H 11.16, 11.21. $C_{12}H_{18}$. Calculated %: C 88.82; H 11.18.

1,4-Dimethyl-2,3-diethylbenzenesulfonamide (not described in the literature) was obtained by the usual procedure (action of chlorosulfonic acid on the hydrocarbon in chloroform solution followed by interaction of the resulting sulfochloride with ammonia) [11]; m.p. 140° (from dilute alcohol).

Found %: N 5.90, 5.80. $C_{12}H_{19}O_2NS$. Calculated %: N 5.80.

1,2,5-Trimethyl-3,4-diethylbenzene (V). Interaction of 2,3,6-trimethyl-4,5-diethyl-1,2,3,6-tetrahydrophthalic anhydride [(II), 43 g, 0.17 mole] with phosphorus pentoxide (25.1 g, 0.17 mole) was effected under the conditions described for reaction of adduct (I) with phosphorus pentoxide. Distillation over sodium gave 26.7 g (89%) of 1,2,5-trimethyl-3,4-diethylbenzene (not described in the literature) with the following constants (after distillation from a column).

B.p. 110.5-111° (9 mm), $n^{20}D$ 1.5192, d^{20}_4 0.9034, MR_D 59.24. $C_{13}H_{20}F_3$. Calculated 58.63, EM_D 0.61.
Found %: C 88.51, 88.43; H 11.51, 11.58. $C_{13}H_{20}$. Calculated %: C 88.57; H 11.43.

1,2,5-Trimethyl-3,4-diethylbenzenesulfonamide (not described in the literature) melted at 115-117° (from dilute alcohol).

1,2,3,4-Tetramethyl-5,6-diethylbenzene (VI). 1,2,3,6-Tetramethyl-4,5-diethyl-1,2,3,6-tetrahydrophthalic anhydride [(III), 21 g, 0.08 mole] and phosphorus pentoxide (11.4 g, 0.08 mole) were placed in a 100 ml round-bottomed flask fitted with a reflux condenser; the reaction mixture was heated 10 hours (until carbon monoxide ceased to come off) and the resulting hydrocarbon was distilled off in vacuo. Possible traces of unreacted adduct were eliminated by dissolving the hydrocarbon in ligroine and heating for 6 hours with concentrated sodium hydroxide solution (in a flask with a reflux condenser). After working up in the usual manner and distillation of the ligroine, the 1,2,3,4-tetramethyl-5,6-diethylbenzene (not described in the literature) was boiled over sodium and distilled in vacuo (yield 11 g, 77%).

B.p. 92-94° (4 mm), $n^{20}D$ 1.5312, d^{20}_4 0.9298, MR_D 63.34. $C_{14}H_{22}$ F_3. Calculated 63.25.
Found %: C 88.56, 88.38; H 11.46, 11.62. $C_{14}H_{22}$. Calculated %: C 88.35; H 11.65.

SUMMARY

1. The behavior of 3,4-diethyl-2,4-hexadiene in the diene synthesis was studied for the first time and its adducts (previously undescribed) with maleic, methylmaleic and dimethylmaleic anhydrides were prepared.

2. Aromatization of these adducts by heating with phosphorus pentoxide gave the previously undescribed polymethyldiethylbenzenes: 1,4-dimethyl-2,3-diethylbenzene (yield 71%), 1,2,5-trimethyl-3,4-diethylbenzene (yield 89%), and 1,2,3,4-tetramethyl-5,6-diethylbenzene (yield 77%).

3. A procedure was developed for preparation of the pinacone of diethyl ketone (3,4-diethyl-3,4-hexanediol) by reduction of diethyl ketone with magnesium amalgam in presence of a little methyl iodide.

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SYNTHESIS OF γ-HALOSUBSTITUTED 1,2,5-TRIMETHYL-, 2,5-DIMETHYL-AND 1-ACYL-2,5-DIMETHYLPIPERIDINES

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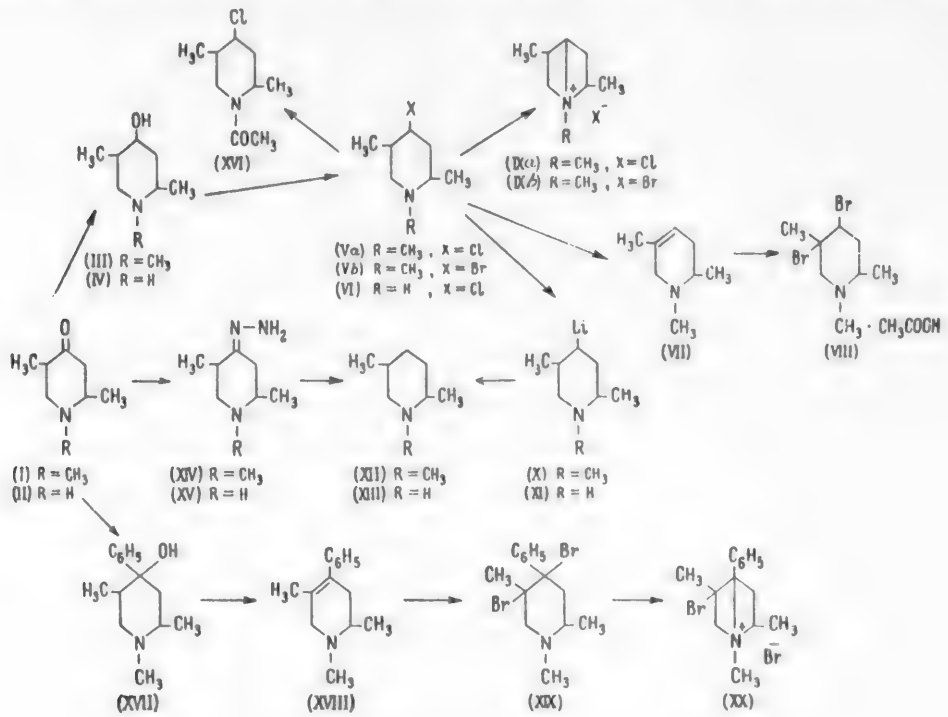
The literature contains very scanty information about the chemistry of γ-halosubstituted piperidines. 1-Methyl-4-chloropiperidine [1] has been the most closely studied. It is isolated in the form of the hydrochloride and in the form of the free base but contaminated by the product of dehydrochlorination.

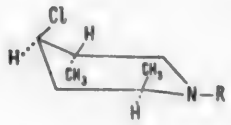
Having at our disposal a convenient method of synthesis of secondary and tertiary γ-piperidols [2], we turned our attention to a study of the substitution of the hydroxy group of these piperidinic alcohols by halogen. The compounds selected for investigation were 1,2,5-trimethyl-(III) and 2,5-dimethyl-(IV)-piperidols, which are formed on reduction of 1,2,5-trimethyl-(I) and 2,5-dimethyl-(II)-4-piperidones respectively. 1,2,5-Trimethyl-4-chloro-(Va) and 2,5-dimethyl-4-chloro-(VI)-piperidines were obtained in a yield of up to 70% by treatment of the respective piperidols with thionyl chloride. In this fashion a mixture of stereoisomeric 1,2,5-trimethyl-4-piperidols (III), obtained by reduction of piperidone (I) with sodium and alcohol, is converted into a mixture of stereoisomeric 1,2,5-trimethyl-4-chloropiperidines (Va) with a predominant content (approx. 70%) of one of the isomers which was identified in the form of the picrate with m.p. 198-200°. The same isomer of chloride (Va)



was prepared from 1,2,5-trimethyl-4-piperidol with m.p. 72-73°. The latter was isolated from a mixture of the stereoisomeric piperidols (III) in which it was likewise present to the extent of approximately 70%. Evidently in this case the replacement of the hydroxy group by chlorine does not result in rotation of the piperidine ring at the γ-carbon atom. 2,5-Dimethyl-4-chloropiperidine (VI) was similarly prepared. Treatment with acetic anhydride converted it into 1-acetyl-2,5-dimethyl-4-chloropiperidine (XVI). 1,2,5-Trimethyl-4-bromopiperidine (Vb) was isolated on treatment of piperidol (III) with phosphorus tribromide.

Halogenated (Va) and (Vb) are mobile liquids which distil in vacuo. They cannot be distilled at atmospheric pressure. On keeping, and also on heating to above 130°, they change into hygroscopic, ether-insoluble products which are evidently inner-molecular salts of quaternary ammonium bases (IXa) and (IXb).

1,2,5-Trimethyl-4-chloropiperidine (Va) was dehydrochlorinated with the help of 25% alcoholic potassium hydroxide. The resulting 1,2,5-trimethyl-1,2,3,6-tetrahydropyridine (VII) was brominated in acetic acid to 1,2,5-trimethyl-4,5-dibromopiperidine which was separated as the acetate (VIII). The halogen in the γ-position of the piperidine ring of these compounds is relatively inert, possibly due to the influence of the amino nitrogen of the piperidine ring. It was not possible to replace the chlorine in this compound by various functional groups in reactions with potassium cyanide, sodium hydrosulfide, diphenylacetonitrile, sodium ethyl acetoacetate, etc. In all of these cases the original halogenated derivative was recovered in admixtures with the product of its dehydrochlorination. Under the usual conditions 1,2,5-trimethyl-(Va) and 2,5-dimethyl-(VI) 4-chloropiperidines do not react with magnesium, but they react with lithium, particularly energetically in the case of chloride (Va). Decomposition with water of the resulting organolithium derivatives (X) and (XI) gave 1,2,5-trimethylpiperidine (XII) and 2,5-dimethylpiperidine (XIII). The latter are also obtained from the hydrazones (XIV) and (XV) of the corresponding piperidones by the Kizhner reaction.



An attempt was made to replace the hydroxy group of the tertiary piperidinic alcohol 1,2,5-trimethyl-4-phenyl-4-piperidol (XVII) by halogen with the help of halogenated phosphorus compounds, thionyl chloride, and hydrogen halides. In all cases, however, in place of a halogenated derivative we obtain the product of dehydration of piperidol (XVII) – 1,2,5-trimethyl-4-phenyl-1,2,3,6-tetrahydropyridine (XVIII) [3]. Bromine can only be made to combine at the unsaturated bond of (XVIII) if a salt is brought into reaction and not the free base of (XVIII). 1,2,5-Trimethyl-4-phenyl-4,5-dibromopiperidine (XIX) was obtained by bromination of the hydrochloride and also of the sulfate of 1,2,5-trimethyl-4-phenyl-1,2,3,6-tetrahydropyridine. The free base of the dibromide (XIX) can be isolated from the salt with weak caustic alkalies in the cold. It is readily soluble in ether, benzene, and other organic solvents. But even on gentle heating, or when stored, it changes into the inner-molecular salt of the quaternary ammonium base (XX) which is insoluble in ether and benzene but easily soluble in water.

EXPERIMENTAL

1,2,5-Trimethyl-4-chloropiperidine (Va). a) To a solution of 25 g of a mixture of stereoisomeric 1,2,5-trimethyl-4-piperidols (III) (b.p. 85-87° at 3 mm) in 100 ml anhydrous benzene was added, with stirring and cooling to 0°, 32 ml thionyl chloride dissolved in 40 ml benzene. After 2 hours' heating at 60-70°, the benzene and excess thionyl chloride were distilled off in vacuo. The residue was dissolved in water and treated with sodium carbonate in presence of ether. The organic bases were extracted with ether and after drying they were distilled in vacuo. There was obtained 19.5 g (Va) in the form of a readily mobile, colorless liquid:

B.p. 44-46° at 2 mm, $n^{20}D$ 1.4710, d^{20}_{20} 0.9895, MR_D 45.59; calc. 45.75.

From 3.5 g (Va) was obtained 6.8 g picrate from which by crystallization from aqueous alcohol was isolated 4.5 g picrate with m.p. 198-200°, corresponding to one of the stereoisomeric forms of (Va).

Found %: N 14.57, 14.65. $C_{14}H_{19}O_7N_4Cl$. Calculated %: N 14.34.

There was also obtained 1.9 g picrate with m.p. 154-164°, corresponding to a mixture of stereoisomeric chlorides (Va).

Found %: N 14.18, 14.45. $C_{14}H_{19}O_7N_4Cl$. Calculated %: N 14.34.

1,2,5-Trimethyl-4-chloropiperidine hydrochloride has m.p. 184-185° (from acetone).

Found %: N 7.37, 6.99, 6.92, 7.30. $C_8H_{17}NCl_2$. Calculated %: N 7.07.

b) To 50 ml thionyl chloride at 0° was added, with stirring, a solution of 10 g 1,2,5-trimethyl-4-piperidol (m.p. 72-73°) in 35 ml benzene. After being heated for 2 hr, the mixture was worked up as described above to give 8.5 g (Va) with b.p. 78-79° at 12 mm. The picrate melted at 198-200° and no depression was observed in a mixed melting test with the specimen described above. Heating of chloride (Va) to 150-180° converted it into an ether-insoluble product.

1,2,5-Trimethyl-4-bromopiperidine (Vb). a) 5 g 1,2,5-Trimethyl-4-piperidolhydrobromide (m.p. 212-213°) was added to 16 g phosphorus pentabromide in 10 ml dioxane at 0-5°. The mixture was stirred 2 hr at room temperature and 3 hr at 80°. A precipitate (3.1 g) of the hydrobromide of (Vb) came down on cooling: m.p. 166-168°.

Found %: N 4.72, 5.02. $C_8H_{17}NBr_2$. Calculated %: N 4.89.

The free base of 1,2,5-trimethyl-4-bromopiperidine was obtained by treatment of an aqueous solution of the hydrobromide with 10% ammonia solution. The picrate melted at 178-180°.

Found %: N 13.15, 13.17. $C_{14}H_{19}O_7N_4Br$. Calculated %: N 12.88.

b) To 29 g 1,2,5-trimethyl-4-piperidol hydrobromide was added, with stirring and cooling with iced water, 60 ml phosphorus tribromide. The mixture was heated 3 hr at 80°. The excess of phosphorus tribromide was taken off in vacuo and the residue treated with sodium carbonate in presence of ether. Fractional distillation of the products extracted by ether gave 12 g of (Vb):

B.p. 56-58° at 2 mm, $n^{20}D$ 1.4952, d^{20}_4 1.2340, MR_D 48.66; calc. 48.64.

2,5-Dimethyl-4-chloropiperidine (VI). At 0° a solution of 31 ml thionyl chloride in 35 ml benzene was added (in a nitrogen stream) to 20 g of a mixture of the stereoisomeric 2,5-dimethyl-4-piperidols (IV) (b.p. 81-83° at 2 mm) in 150 ml anhydrous benzene. After the mixture had been stirred one hour at room temperature and 2 hours at 80°, the benzene and excess thionyl chloride were distilled off in vacuo. The residue was dissolved in water and treated with sodium carbonate and ether. Fractional distillation of the extracted reaction products gave 12 g of (VI).

B.p. 78-80° at 10 mm, $n^{20}D$ 1.4780, d^{20}_{20} 1.0170, MR_D 40.80; calc. 41.11.

Found %: N 9.51, 9.51. $C_7H_{14}NCl$. Calculated %: N 9.47.

Picrate: m.p. 219-221° (from alcohol).

Found %: N 14.57. $C_{13}H_{17}N_4Cl$. Calculated %: N 14.87.

(VI) crystallized nearly completely when kept. M.p. 36-37° (after washing with benzene).

Found %: N 9.30, 9.38. $C_7H_{14}NCl$. Calculated %: N 9.47.

1-Acetyl-2,5-dimethyl-4-chloropiperidine (XVI). 7 ml acetic anhydride was added to 10 g 2,5-dimethyl-4-chloropiperidine (VI) cooled with iced water. After 8 hours heating, the excess of acetic anhydride was distilled off, and the residue was distilled in vacuo. There was obtained 12 g of (XVI), b.p. 132-133° (2 mm).

Found %: N 7.41, 7.52. $C_9H_{16}ONCl$. Calculated %: N 7.39.

1,2,5-Trimethyl-1,2,3,6-tetrahydropyridine (VII). a) 5 g 1,2,5-trimethyl-4-chloropiperidine and 20 ml 15% potassium hydroxide solution were heated 4 hours on a boiling water bath. The reaction mixture was then treated with 18% hydrochloric acid (Congo test), the alcohol was driven off in vacuo, the residue was treated with potassium hydroxide and the reaction products extracted with ether. Distillation gave 2.5 g of (VII) with b.p. 53-56° at 2 mm, $n^{20}D$ 1.4608.

Picrate: m.p. 135-137°.

Found %: N 15.88, 15.68. $C_{14}H_{18}O_7N_4$. Calculated %: N 15.82.

b) 7 g 1,2,5-trimethyl-4-bromopiperidine and 40 ml 25% potassium hydroxide solution were heated 5 hours at the boiling point of alcohol. The mixture was worked up as described above and gave 3 g of (VII); b.p. 55-56° at 2 mm, $n^{20}D$ 1.4600. Picrate: m.p. 135-137°; no depression in admixture with the specimen described above.

1,2,5-Trimethyl-4,5-dibromopiperidine acetate (VIII). A solution of 2.7 ml bromine in 15 ml acetic acid was added dropwise to a solution of 4.5 g 1,2,5-trimethyl-1,2,3,6-tetrahydropyridine in 13 ml acetic acid. After the excess of acetic acid had been driven off, the residue crystallized. There was isolated 5 g of acetate (VIII) with m.p. 148-151° (decomp.) (from acetone).

Found %: N 4.39, 4.37. $C_{10}H_{19}O_2NBr_2$. Calculated %: N 4.06.

1,2,5-Trimethylpiperidine (XII). a) 5 g 1,2,5-trimethyl-4-chloropiperidine was added with cooling to 0.5 g lithium and 100 ml ether. After 4-hours' stirring at room temperature, which was accompanied by heat development and separation of a green precipitate, the reaction product was treated with 50 ml water. The ether layer was collected and dried. Distillation of the reaction product gave 2.2 g (XII); b.p. 146-147°, $n^{20}D$ 1.4445. Picrate: m.p. 173-175°.

Found %: N 15.32, 15.35. $C_{14}H_{20}O_7N_4$. Calculated %: N 15.72.

b) A mixture of 15 g 1,2,5-trimethyl-4-piperidone and 17.5 g hydrazine hydrate was heated 0.5 hours on a boiling water bath. The excess of hydrazine hydrate was distilled off in vacuo and the residue was distilled to give 5.4 g 1,2,5-trimethyl-4-piperidone (110-120° at 2 mm). The latter was heated to 200° with 4 g potassium hydroxide in powder form. Heating was accompanied by violent evolution of nitrogen and by distillation at 120-150° of the reaction products. Redistillation yielded 2.5 g of (XII) with b.p. 173-175°. A picrate was prepared with m.p. 173-175° which did not give a depression in admixture with the above-described specimen. The synthesis of 2,5-dimethylpiperidine (XIII) has already been described [4].

1,2,5-Trimethyl-4,5-dibromo-4-phenylpiperidine (XIX). a) To a solution of 1.6 g 1,2,5-trimethyl-4-phenyl-1,2,3,6-tetrahydropyridine hydrochloride (m.p. 185-187°) in 10 ml of glacial acetic acid was added, with stirring and cooling, a solution of 0.4 ml bromine in 10 ml acid. The acetic acid was driven off in vacuo. From the residue was isolated 2.4 g 1,2,5-trimethyl-4,5-dibromo-4-phenylpiperidine hydrochloride, m.p. 154° with decomp. (from acetone).

Found %: N 3.84, 3.96. $C_{14}H_{20}NClBr_2$. Calculated %: N 3.52.

b) 30 ml water and 2.2 g sulfuric acid (dissolved in 20 ml water) were run into 9.1 g 1,2,5-trimethyl-4-phenyl-1,2,3,6-tetrahydropyridine. The aqueous solution was washed with ether, then evaporated to dryness in vacuo and dried in a vacuum-desiccator. To the solution of the resultant sulfate in 150 ml glacial acetic acid was added, dropwise with cooling, a solution of 2.3 ml bromine in 50 ml acetic acid. The color of bromine disappeared. At the bottom of the flask appeared an oil from which, the precipitation with ether from acetone solution, was isolated 2.6 g of the sulfate of 1,2,5-trimethyl-4,5-dibromo-4-phenylpiperidine with m.p. 147° (with decomp.).

Found %: N 3.32, 3.04. $C_{28}H_{40}O_4N_2SBr_4$. Calculated %: N 3.41.

The aqueous solution of 0.5 g of the sulfate was treated with 5% sodium carbonate solution in presence of ether. The ethereal extract was dried with sodium sulfate in the cold. Removal of the ether (without heat) left 0.3 g of (XIX) in the form of crystals with m.p. 88-95°, readily soluble in ether and benzene. Gentle heating or storage of the benzene solution led to separation of crystals which quickly turned brown in the air and deliquesced. This precipitate was evidently the inner-molecular salt of the quaternary ammonium base (XX). It was insoluble in ether and benzene.

SUMMARY

1,2,5-Trimethyl-4-chloropiperidine and 2,5-dimethyl-4-chloropiperidine were prepared. Some of their chemical transformations were studied.

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INVESTIGATIONS ON BENZIMIDAZOLE DERIVATIVES

III. REACTION OF COMPOUNDS OF THE BENZIMIDAZOLE SERIES WITH NUCLEOPHILIC REAGENTS

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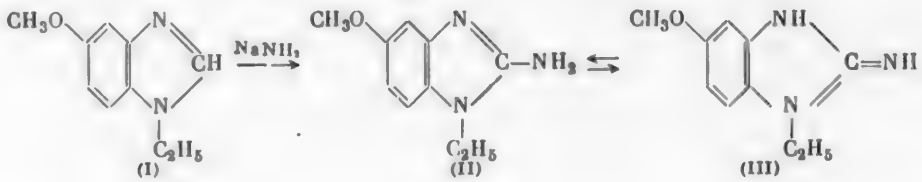
The reaction of nucleophilic substitution in the benzimidazole series has scarcely been studied. Some years ago one of us in collaboration with Uglov [1] carried out the amination of 5-methoxy-1-methylbenzimidazole by reacting it with sodium amide. We were interested in continuing this work by studying the action of sodium amide as well as of other nucleophilic reagents on benzimidazole and some of its N-substituted derivatives.

Our experiments showed that 5-ethoxy-1-benzimidazole (I) resembled the 5-methoxy-1-methyl derivative in facility of amination when heated with sodium amide. It was converted into 2-amino-5-methoxy-1-ethylbenzimidazole (II). The reaction is performed in dimethylaniline and a yield of 60% is attained. The new compound possibly exists as a second tautomeric form – 5-methoxy-1-ethylbenzimidazoloneimine (III) [10]. The question of the tautomerism of compounds of this type merits special attention.



Unlike the 1-alkyl derivatives, benzimidazole itself could not be converted into an amino derivative by the action of sodium amide.* These results may be explained by the following considerations. Under the experimental conditions benzimidazole is at first converted into a salt-like compound [2]; an anionic charge is developed in the imidazole ring, and the carbon atom in the 2-position loses the ability to react with a second molecule of reagent.

We know that N-alkyl and N-phenyl derivatives of benzimidazole cannot be aminated with hydroxylamine [4] which is a weaker nucleophilic reagent than sodium amide. Starting from the assumption that the introduction of an arylsulfonyl group into the NH group of benzimidazole will lower the electron density in the 2-position of the imidazole ring and will therefore increase the susceptibility of the resulting derivative to nucleophilic substitution, we attempted to aminate 1-benzenesulfonylbenzimidazole with the help of hydroxylamine. The experiments were unsuccessful under various conditions just as they were in the case of 1-(2',4'-dinitrophenyl)-benzimidazole [5]. Only benzimidazole benzenesulfonate could be isolated from the reaction medium.

*5-Methoxybenzimidazole also is not aminated by sodium amide [3].

Formation of a benzimidazole salt is the result of hydrolysis of the original compound under the experimental conditions, since the bond between the arylsulfonyl group and the N atom of the imidazole ring of benzimidazole is extremely weak. For example it is easily cleaved, as shown earlier [6], by the action of dilute hydrochloric acid, and (as we found) by reaction with aromatic amines. Especially susceptible to hydrolysis, even on heating of its aqueous alcoholic solution, is 1-(p-nitrobenzenesulfonyl)-benzimidazole.

EXPERIMENTAL

2-Nitro-4-methoxy-N-ethylanilide of benzenesulfonic acid. 1.2 g of sodium was dissolved in 30 ml alcohol. Into the solution were charged 12 g benzenesulfonic acid 2-nitromethoxyanilide [7] and 14 ml ethyl iodide, and the mixture was refluxed 4 hours. A precipitate appeared on cooling and was filtered and washed with alcohol. Yield 12.1 g (92%). White crystals (from alcohol), m.p. 67-68°.

Found %: N 8.26, 8.17; S 9.46, 9.40. $C_{15}H_{16}O_5N_2S$. Calculated %: N 8.33; S 9.53.

3-Nitro-4-ethylaminoanisole. 10 g benzenesulfonic acid 2-nitro-4-methoxy-N-ethylanilide was gradually added to 25 ml sulfuric acid (d 1.84). The next day the solution was heated half an hour at 60° and poured into 250 ml water. The precipitate was filtered. Yield nearly quantitative. Bright-red crystals (from alcohol) with m.p. 59-60°, soluble in benzene and acetone.

Found %: N 14.36, 14.14. $C_9H_{12}O_3N_2$. Calculated %: N 14.28.

5-Methoxy-1-ethylbenzimidazole. 6 g 3-nitro-4-ethylaminoanisole and 10.0 g tin were heated in 80 ml hydrochloric acid (1:1) on a water bath until the tin had nearly completely dissolved. The cooled mass was treated with excess of 10% sodium hydroxide. The tin hydroxide was filtered off and the diamine was extracted from the filtrate with benzene and from the precipitate with alcohol. The benzene layer was shaken with formic acid. The acid layer was separated and into it was charged the residue resulting from removal of the alcohol from the alcoholic extract. The mixture was heated 2 hours on a boiling water bath, diluted with water and made alkaline with sodium hydroxide (40%). The benzimidazole derivative separated in the form of an oil and was extracted with chloroform. The extract was dried with sodium sulfate. The chloroform was distilled off and the residue twice distilled in vacuo. B.p. 188-190° at 2 mm. M.p. 48-49°. White, very hygroscopic crystals, easily soluble in all of the usual solvents except ligroine.

Found %: N 15.69, 15.99. $C_{10}H_{12}ON_2$. Calculated %: N 15.90.

Picrate: light-yellow crystals (from glacial acetic acid) with m.p. 230-231°.

2-Amino-5-methoxy-1-ethylbenzimidazole. 1 g sodium was dissolved in 50 ml liquid ammonia in presence of 0.03 g crystalline iron nitrate [8], and 30 ml dry dimethylaniline was added. While the ammonia was evaporating, 6 g 5-methoxy-1-ethylbenzimidazole was added to the mixture which was then mechanically stirred and heated to 115°. Heating was continued at this temperature until hydrogen ceased to come off (1-1.5 hours.) To the mass were added 2 ml water and 40 ml toluene with stirring. After cooling, the precipitate was filtered. Yield 4.0 g (61%). White crystals (from benzene) with m.p. 170-171°.

Found %: N 21.79, 21.85. $C_{10}H_{13}ON_3$. Calculated %: N 21.97.

2-(p-Nitrobenzylideneamino)-5-methoxy-1-ethylbenzimidazole. A solution of 0.4 g 2-amino-5-methoxy-1-ethylbenzimidazole and 0.40 g p-nitrobenzaldehyde in 7 ml alcohol was boiled 2 hours. Azomethine came down when the solution was cooled. Orange-red crystals (from alcohol) with m.p. 178.5-179.5°. Yield 0.61 g (90%).

Found %: N 17.12, 17.45. $C_{17}H_{16}O_3N_4$. Calculated %: N 17.28.

Experiments on the amination of benzimidazole with sodium amide. 3 g benzimidazole and sodium amide, prepared as described above from 1.4 g sodium, were heated in 25 ml dry dimethylaniline for 2.5 hours with mechanical stirring at 115°.* The cooled mass was carefully worked up with 15 ml water. The resultant white precipitate was filtered off, washed with water and dried (0.9 g). The layers were separated, the aqueous layer was evaporated to $\frac{1}{4}$ of its volume and the white precipitate was filtered off (1.2 g). Treatment of the filtrate with ammonium chloride yielded a further 0.8 g white precipitate. A mixture of a sample of each of these products with benzimidazole did not exhibit a depression of melting point. The total yield of benzimidazole from the reaction mixture was therefore 2.9 g or 96% of the quantity taken.

*Evolution of hydrogen was not observed during this operation.

1-Benzenesulfonylbenzimidazole. A solution of 20 g benzenesulfochloride in 15 ml dry pyridine was run into a solution of 12 g benzimidazole in 35 ml dry pyridine. On the following day 180 ml water was added to the mixture; the precipitate was filtered, washed with 2% sodium hydroxide solution and with water and then dried at room temperature. Yield 26 g (nearly quantitative). Snow-white crystals (from alcohol) with m.p. 106-107°, easily soluble in ether and benzene.

Found %: N 11.09, 10.96; S 12.47, 12.52. $C_{13}H_{10}O_2N_2S$. Calculated %: N 10.85; S 12.41.

Picrate: light-yellow crystals with m.p. 120-121° (from alcohol).

Found %: N 14.42. 14.23. $C_{13}H_{10}O_2N_2S \cdot HOC_6H_2(NO_2)_3$. Calculated %: N 14.37.

1-(p-Nitrobenzenesulfonyl)-benzimidazole. The compound was prepared by a procedure similar to that employed for 1-benzenesulfonylbenzimidazole in 75% yield. White crystals (from dry toluene) with m.p. 160°. Hydrolysis takes place with facility when the alcoholic solution is heated, and benzimidazole is formed.

Found %: S 10.68, 10.42. $C_{13}H_9O_4N_3S$. Calculated %: S 10.57.

Interaction of 1-benzenesulfonylbenzimidazole with aniline. A solution of 0.3 g 1-benzenesulfonylbenzimidazole in 2 g aniline was heated 4 hours on a boiling water bath. The cooled mass was treated with 1.5 ml dilute (1:2) hydrochloric acid. The precipitate of benzenesulfanilide was filtered, washed with water, and crystallized from alcohol. M.p. 108-109°. Yield 0.2 g (74%). A mixture with authentic benzenesulfanilide did not give a depression of melting point.

Experiments on the amination of 1-benzenesulfonylbenzimidazole with hydroxylamine. 2 g hydroxylamine hydrochloride and 2 g crystalline sodium acetate were heated in 30 ml alcohol. The precipitate was filtered. Into the filtrate was introduced 5 g 1-benzenesulfonylbenzimidazole, and the solution was boiled 6 hours. After nearly the whole of the alcohol had been driven off from the solution, white crystals separated. Yield 4.8 g. Melting point 217-218°. They were readily soluble in water and alcohol. Benzimidazole picrate came down when these solutions were treated with picric acid in the cold. It would thus appear that the product obtained was a salt of benzimidazole. Comparison with authentic benzimidazole benzenesulfonate confirmed their identity. Consequently, under the experimental conditions 1-benzenesulfonylbenzimidazole is not aminated and only undergoes hydrolysis.

Found %: S 11.50. $C_7H_6N_2 \cdot C_6H_5SO_3H$. Calculated %: S 11.60.

1-Benzenesulfonylbenzimidazole is also not susceptible to amination by hydroxylamine in pyridine at 110° and in an aqueous medium in presence of excess of caustic alkali (compare the preparation of aminobenzothiazole by Skraup's method [4, 9]).

SUMMARY

1. Earlier studies of the reaction of benzimidazole derivatives with sodium amide were continued. It was established that 5-methoxy-1-ethylbenzimidazole is easily converted into the 2-amino derivative by the action of sodium amide in dimethylaniline solution.

2. Compounds of the benzimidazole series containing an unsubstituted NH group are not aminated by sodium amide.

3. It was shown that 1-benzenesulfonylbenzimidazole does not react with hydroxylamine; under the experimental conditions the starting compound is hydrolyzed with the formation of benzimidazole benzenesulfonate.

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SYNTHESIS ON THE BASIS OF THE ETHYL ESTER OF HYDROXYMETHYLPHOSPHINIC ACID

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The sodium derivative of the ethyl ester of hydroxymethylphosphinic acid $(C_2H_5O)_2POCH_2ONa$(I) proved to be the most convenient for the performance of synthesis. This compound is very readily accessible [1]. A study was made of its reactions with diethylphosphoryl chloride, ethyl chloroacetate, ethyl chloroformate, 2-chloroethanol, silicon tetrachloride, phosphorus trichloride, carbonyl chloride, and thionyl chloride.

The first four reactions went normally with formation of the expected compounds. The product of reaction with diethylphosphoryl chloride was the diethylphosphoric ester of the ethyl ester of hydroxymethylphosphinic acid:

$$(C_2H_5O)_2POCl + NaOCH_2PO(OC_2H_5)_2 \rightarrow (C_2H_5O)_2POCH_2OPO(OC_2H_5)_2 + NaCl.$$

The product of the reaction with ethyl chloroacetate was α-diethylphosphono-α'-carbethoxydimethyl ether:

$$ClCH_2COOC_2H_5 + NaOCH_2PO(OC_2H_5)_2 \rightarrow (C_2H_5O)_2POCH_2OCH_2COOC_2H_5 + NaCl.$$

With ethyl chloroformate the reaction

$$(C_2H_5O)_2POCH_2ONa + ClCOOC_2H_5 \rightarrow (C_2H_5O)_2POCH_2OCOOC_2H_5 + (C_2H_5O)_2CO + NaCl$$

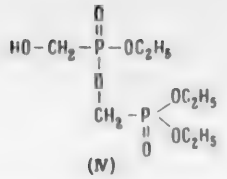
gave a product which on subsequent distillations breaks down, loses CO_2 and approximates in composition to the ethyl ester of ethoxymethylphosphinic acid $(C_2H_5O)_2POCH_2OC_2H_5$ [2]. Diethyl carbonate is also isolated in this reaction.

With 2-chloroethanol the reaction yielded a substance whose analysis corresponded to the ethyl ester of hydroxymethylphosphinic acid. Reaction with silicon tetrachloride and phosphorus trichloride did not give well-defined products with the exception of the ethyl ester of hydroxymethylphosphinic acid which was obtained in both cases. Reaction with carbonyl chloride gave a liquid product whose analysis corresponded neither to (II) or (III) but approached closer to (II):

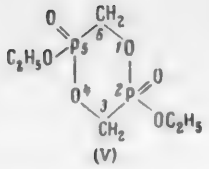
$$COCl_2 + 2NaOCH_2PO(OC_2H_5)_2 \rightarrow (C_2H_5O)_2POCH_2OCOOCH_2PO(OC_2H_5)_2 \quad \text{(II)}$$

$$(C_2H_5O)_2POCH_2OCH_2PO(OC_2H_5)_2 \quad \text{(III)}$$

The most interesting and complex reaction was that with thionyl chloride. Several products were isolated: diethyl sulfite, triethyl phosphate, the ethyl ester of hydroxymethylphosphinic acid and two more products – a liquid with the empirical formula $C_8H_{20}O_7P_2$ and a white crystalline substance with m. p. 150-151° and the empirical formula $C_6H_{14}O_6P_2$. After prolonged standing in a sealed tube, the liquid compound deposited crystals with m. p. 150-151°. To the liquid compound we provisionally assign the structure of (IV) – a mixed ethyl (diethylphosphono)-methyl ester of hydroxymethylphosphinic acid. The crystalline product corresponds to Formula (V) – 1,4-dioxa-2,5-epoxy-2,5-diethoxy 2,5-diphosphorinan [3].

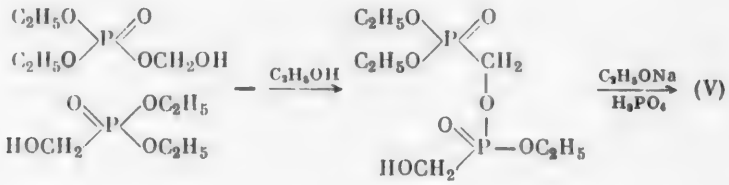


(IV)



(V)

The liquid product (IV) could have been formed from the ethyl ester of hydroxymethylphosphinic acid by loss of a molecule of alcohol from two molecules of ester. Further loss of a molecule of ethyl alcohol could lead to the cyclic product (V).



The structure of the crystalline product (V) was confirmed by its synthesis by ring closure from two molecules of the ethyl ester of hydroxymethylphosphinic acid or of its acetate by boiling with sodium alkoxide or phosphoric acid. Ring closure was successfully effected by prolonged boiling with sodium alkoxide but boiling with phosphoric acid did not give satisfactory results.

The acetate of the ethyl ester of hydroxymethylphosphinic acid was prepared from chloromethyl acetate and triethyl phosphite.

$$CH_3COOCH_2Cl + P(OC_2H_5)_3 \rightarrow C_2H_5Cl + CH_3COOCH_2PO(OC_2H_5)_2.$$

Boiling of the acetate with sodium alkoxide or phosphoric acid gave product (V). This acetate could not be obtained pure by reaction of the sodium derivative of the ethyl ester of hydroxymethylphosphinic acid with acetyl chloride due to decomposition in course of distillation.

EXPERIMENTAL

Sodium derivative of the ethyl ester of hydroxymethylphosphinic acid (I). 2.3 g finely sliced metallic sodium was added to 50 ml dry ether, and 14 g diethylphosphorous acid was added dropwise. After the whole of the sodium had disappeared, the solution was cooled and 3 g polyoxymethylene was rapidly dropped into it. A violent reaction commenced and the whole of the polyoxymethylene reacted. The transparent liquid was an ethereal solution of the sodium derivative of the ethyl ester of hydroxymethylphosphinic acid. It was used in that form for further reactions.

Reaction of (I) with diethylphosphoryl chloride. To the sodium derivative (I) prepared from the above quantities of components was added dropwise 19 g diethyl phosphoryl chloride. A violent reaction ensued and sodium chloride came down. After the ether and the NaCl had been separated, the solution was distilled in vacuo. Three distillations gave the diethylphosphoric ester of the ethyl ester of hydroxymethylphosphinic acid (7 g, 23%):

B.p. 162.5-163.5° (1.5 mm), d^{20}_{20} 1.1776, $n^{20}D$ 1.4283.

Found %: C 35.85; H 7.48; P 20.8, 20.97. $C_9H_{22}O_7P_2$. Calculated %: C 35.57; H 7.24; P 20.39.

Subsequent fractionation of the product led to decomposition with separation of a fraction boiling at 74-76° (2-3 mm) whose composition did not correspond to that of any known product. Its structure was not established.

Reaction of (I) with the ethyl ester of monochloroacetic acid. Dropwise addition of 24.5 g ethyl monochloroacetate was made to an ethereal solution of the sodium derivative of (I) (prepared from 28 g diethylphosphorous acid, 4.6 g metallic sodium, 80 ml absolute ether and 6 g polyoxymethylene). The reaction was violent.

The reaction mixture was heated 1 hour on a water bath. After the sodium chloride had been separated and the ether driven off, the liquid product was distilled. The following fractions were obtained after two distillations:

1st, b.p. 80-144° (2.5 mm), $n^{20}D$ 1.4170, 1.55 g; 2nd, b.p. 144-147° (1.5 mm), $n^{20}D$ 1.4340, d^{20}_{20} 1.1410, 2.7 g; 3rd, b.p. 147-149° (1.5 mm), $n^{20}D$ 1.4348, d^{20}_{20} 1.1496, 21.85 g. Residue 15.1 g.

The 3rd fraction corresponded to α-diethylphosphono-α'-carbethoxydimethyl ether. Yield 43%.

Found %: C 42.85, 42.73; H 7.64, 7.52; P 12.11, 11.98. $C_9H_{19}O_6P$. Calculated %: C 42.52; H 7.44; P 12.2.

Reaction of (I) with ethyl chloroformate. 21.7 g ethyl chloroformate was added dropwise to an ethereal solution of the sodium derivative (I) prepared from 28 g diethylphosphorous acid, 4.6 g metallic sodium, 6 g polyoxymethylene and 100 ml absolute ether. After 2 hours' heating on a water bath, the sodium chloride was centrifuged off, the ether was distilled off, and the filtrate was distilled in vacuo. The following fractions were collected after two distillations:

1st, b.p. 124-127.5° (760 mm), $n^{20}D$ 1.3837, d^{20}_{20} 0.9760, 8.3 g; 2nd b.p. 152° (11.5 mm), 4 g; 3rd b.p. 152-153° (11.5 mm), $n^{20}D$ 1.4215, d^{20}_{20} 1.1246, 8.5 g (17.24%). The residue after distillation consisted of 10.3 g viscous, transparent oil.

The 1st fraction corresponds to diethyl carbonate.

Found %: C 51.45, 51.18; H 8.16, 7.87; trace of P. $C_5H_{10}O_3$. Calculated %: C 50.85; H 8.45.

The 3rd fraction was the carbethoxy ester of the ethyl ester of hydroxymethylphosphinic acid.

Found %: C 40.04, 39.86; H 7.01, 7.09; P 12.57, 12.37. $C_8H_{17}O_6P$. Calculated %: C 40.0; H 7.01; P 12.91.

Subsequent fractional distillations led to breakdown of the ester, and a stable fraction was isolated with b.p. 68° (4 mm), $n^{20}D$ 1.4150, d^{20}_{20} 0.9032, and a fraction with b.p. 129-130° (2 mm), $n^{20}D$ 1.4265, d^{20}_{20} 0.8629; the latter approximated in composition to the ethyl ester of ethoxymethylphosphinic acid.

Found %: C 40.38, 39.88; H 7.6, 7.52; P 14.21, 14.44. $C_7H_{17}O_4P$. Calculated %: C 41.88; H 8.68; P 15.81.

Reaction of (I) with 2-chloroethanol. 2-Chloroethanol (b.p. 127-128.5°) [4] was run into an ethereal solution of the sodium derivative (I) prepared from 28 g diethylphosphorous acid, 4.6 g metallic sodium, 6 g polyoxymethylene and 100 ml dry ether. The reaction went without much outward change. The mass was heated 2 hours on a water bath. The sodium chloride was filtered off and the filtrate was distilled in vacuo. After two distillations a fraction was collected with b.p. 141-141.5° (4 mm), $n^{20}D$ 1.4370, d^{20}_{20} 1.1700. This approximated to the ethyl ester of hydroxymethylphosphinic acid. The ester decomposed in subsequent distillations.

Reaction of (I) with silicon tetrachloride. The reaction was performed with 4 moles sodium derivative (I) and 1 mole $SiCl_4$. It went very violently. The main product was an undistillable residue (a yellow, viscous oil) which later solidified to a crumbly mass. An insignificant quantity of product with b.p. 140.5-141° (4 mm), $n^{20}D$ 1.4325, d^{20}_{20} 1.1527 was collected. Its composition approximated to the ethyl ester of hydroxymethylphosphinic acid.

Reaction of (I) with phosphorus trichloride. 3 moles sodium derivative (I) were reacted with 1 mole PCl_3. The reaction was violent. The main reaction product was the ethyl ester of hydroxymethylphosphinic acid with b.p. 136-138° (3 mm), $n^{20}D$ 1.4283, d^{20}_{20} 1.1380.

Found %: C 35.16, 35.53; H 7.53, 7.65; P 18.39, 18.57. $C_5H_{13}O_4P$. Calculated %: C 35.71; H 7.74; P 18.45.

Low-boiling products approaching diethylphosphorous acid in composition were also isolated.

Reaction of (I) with carbonyl chloride. Carbonyl chloride was passed into an ethereal solution of the sodium derivative at room temperature until heat ceased to be developed and no more sodium chloride was precipitated. The precipitate was filtered and the filtrate was distilled. Several distillations led to collection of a fraction with b.p. 133-136° (1.5 mm), $n^{20}D$ 1.4270, d^{20}_{20} 1.1603. Found %: C 36.61, 36.85; H 7.04, 6.89; P 15.79, 15.63, which corresponds to the empirical formula $C_6H_{15}O_5P$.

Reaction of (I) with thionyl chloride. 10 g $SOCl_2$ was added dropwise to sodium derivative (I) prepared from 24 g diethylphosphorous acid, 3.9 g metallic sodium, 4.8 g polyoxymethylene and 75 ml dry ether. The reaction was very violent and heat was evolved. After the NaCl had been separated, the following fractions were collected from the filtrate:

1) B.p. 48° (6 mm), $n^{20}D$ 1.4140, d^{20}_{20} 1.0840, 1.5 g.
Found %: C 35.29, 35.82; H 7.42, 7.39; S 21.59. $C_4H_{10}O_3S$. Calculated %: C 34.71; H 7.25; S 23.2.

2) B.p. 83-86° (6 mm), $n^{20}D$ 1.4101, d^{20}_{20} 1.0740, 0.45 g.
Found %: C 39.25, 39.41; H 8.43, 8.21; P 17.13. $C_6H_{15}O_4P$. Calculated %: C 39.56; H 8.24; P 17.03.

3) B.p. 138° (3 mm), $n^{20}D$ 1.4325, d^{20}_{20} 1.1448; 1.1 g.
Found %: C 35.33; H 7.84; P 18.28. $C_5H_{13}O_4P$. Calculated %: C 35.71; H 7.74; P 18.45.

4) B.p. 173° (2.5 mm), $n^{20}D$ 1.4360, d^{20}_{20} 1.1947, 1.4 g.
Found %: C 33.34; H 7.02; P 21.07, 21.39. $C_8H_{20}O_7P_2$. Calculated %: C 33.10; H 6.9; P 21.38.

Six months after being sealed into an ampoule, the last fraction deposited small white needles with m.p. 150-151° which did not give a depression of melting point with product 5 from this experiment.

5) White crystals with m.p. 150-151°; yield 0.9 g.
Found %: C 29.46, 29.38; H 5.62, 5.77; P 25.30, 25.24. M 243.8. $C_6H_{14}O_6P_2$. Calculated %: C 29.5; H 5.73; P 25.4. M 244.

Acetate of the ethyl ester of hydroxymethylphosphinic acid. 65 g triethyl phosphite was added dropwise to 42.5 g chloromethyl acetate [5]. The reaction was slightly exothermic. The reaction mixture was heated 4 hours on a water bath and then distilled.

The following fractions were collected at atmospheric pressure: 1st, b.p. 38-63°; 2nd, b.p. 63-112°; 3rd, b.p. 112-115°; 4th, b.p. 115-135°; total weight of fractions 36. g. Vacuum distillation of the residue yielded the following fractions: 1st, b.p. 42° (7 mm), $n^{20}D$ 1.4110, 29 g (resembles triethyl phosphite); 2nd, b.p. 74.5-156° (8 mm), $n^{20}D$ 1.4345, 20.0 g; 3rd, b.p. 154-156° (7 mm), $n^{20}D$ 1.4410, 5.5 g; 4th, b.p. 190-204° (6 mm), 16 g.

Redistillation of the 4th fraction yielded a product with b.p. 180-183° (3 mm), $n^{20}D$ 1.4375, d^{20}_{20} 1.1420, 12 g; a colorless liquid identified as the acetate of the ethyl ester of hydroxymethylphosphinic acid.

Found %: C 40.42, 40.25; H 7.21, 7.15; P 14.68, 14.54. $C_7H_{15}O_5P$. Calculated %: C 40.0; H 7.14; P 14.76.

The compound was unstable. Further fractional distillations gave a high-boiling fraction with b.p. 193-199° (3 mm), $n^{20}D$ 1.4426, d^{20}_{20} 1.1705; empirical formula $C_5H_{11}O_2P$.

Confirmation of structure of the crystalline product with m.p. 150-151°. 1. Boiling of the ethyl ester of hydroxymethylphosphinic acid with sodium alkoxide. Sodium derivative (I) was prepared from 21 g diethylphosphorous acid, 3.45 g metallic sodium, 4.5 g polyoxymethylene in 100 ml absolute ether. 9.16 g glacial acetic acid was added to separate the ethyl ester of hydroxymethylphosphinic acid. The precipitated sodium acetate was filtered off. The filtrate was boiled with 5 drops freshly prepared sodium ethoxide for 3 hours on a water bath. The ether was driven off and the residue was distilled in vacuo to give a fraction with b. p. 63-138° (7.5 mm) and a fraction with b. p. 138-143° (7.5 mm). The second fraction deposited small white needles with m. p. 145-150°; yield 0.5 g. No melting point depression in admixture with the crystalline product described above. A crystalline produce was not isolated after boiling of the ethyl ester of hydroxymethylphosphinic acid with phosphoric acid.

2. Cyclization of the acetate of the ethyl ester of hydroxymethylphosphinic acid prepared from acetyl chloride and the sodium derivative of the ethyl ester of hydroxymethylphosphinic acid. Sodium derivative (I) was prepared from 42 g diethylphosphorous acid, 6.9 g sodium, 9 g polyoxymethylene in 200 ml absolute ether. Into the transparent solution was run 24 g acetyl chloride; heat was developed and sodium chloride came down. After 2-hours' standing, the latter was filtered and washed with ether. A few drops of phosphoric acid were run into the filtrate and the mixture was heated 4 hours on a water bath. Ether and ethyl acetate were distilled off. Yield of ethyl acetate 14.4 g (instead of 28 g). The residue was distilled in vacuo. A fraction with b.p. 105-106° (5 mm) was collected. Further distillation was impossible due to serious breakdown. After 5 weeks, the yellowish, transparent mass was again distilled. Distillation went normally with decomposition at the end. A fraction with b.p. 125-135° (4 mm) was isolated. It deposited white crystals which, after washing with ether, melted at 145-150°. No depression in admixture with the product described above.

3. Cyclization of the acetate of the ethyl ester of hydroxymethylphosphinic acid prepared from chloromethyl acetate and triethyl phosphite. 3 g acetate in a medium of absolute ether was boiled 5 hours on a water

bath in presence of 2 ml freshly prepared sodium ethoxide. The ether was distilled off; the yellowish mass was then distilled and 0.3 g white crystals with m.p. 148-150° was isolated from it. No melting point depression in a mixed test with the product described above.

Found %: P 25.49. $C_6H_{14}O_6P_2$. Calculated %: P 25.4.

Boiling of this acetyl derivative with phosphoric acid likewise leads to separation of the same crystalline product.

SUMMARY

Six new esters were prepared from the ethyl ester of hydroxymethylphosphinic acid: diethylphosphoric acid ester of hydroxymethylphosphinic acid; α-diethylphosphono-α'-carbethoxydimethyl ether; carbethoxy ether of the ethyl ester of hydroxymethylphosphinic acid; acetate of the ethyl ester of hydroxymethylphosphinic acid; mixed ethyl (diethylphosphono) methyl ester of hydroxymethylphosphinic acid; and 1,4-dioxa-2,5-diepoxy-2,5-diethoxy-2,5-diphosphorinan.

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CONTRAPOLARIZED SYSTEMS AND COLOR

I. THE SPECTRA OF SOME DERIVATIVES OF 4-NITROBENZANILIDE CONTAINING SOME ELECTRON-DONATING CHROMOPHORES IN ONE RING

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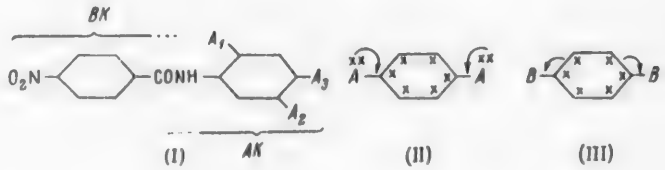
4-Nitrobenzanilides of structure (I), where A_1, A_2 and A_3 are electron-donating groups, are of interest both in connection with the problem of color and with their potential value as intermediates for the synthesis of diamines and direct azo dyes.



(I) (II) (III)

The study of compounds with the structure $O_2N-C_6H_4-CONH-C_6H_4-A$ with para- and meta-position of the NO_2 and A groups [1, 2] led to broadening and clarification of the Kaufmann rule: "two auxochromes in the para-position reinforce one another" [3]. It was established that the presence in the para-position or in even positions in general of a conjugated 1,4- or 1,6-system of not only two electron-donating chromophores* of the type of A, but also of two electronophilic chromophores of the type of B (for example NO_2, CO) [4-6], induces a bathochromic effect. The effect was attributed to the enhanced electron-donating ability in the case of the two A groups (II) and to the intensified electronophilicity of the two B groups (III) due to electronic shifts caused by opposing influences (contrapolarized systems) [4-6].

In the light of the foregoing rule we can expect the color to be intensified on introduction not only of A_3 into the p-position to NH (first donating group) but also of two A_1 and A_2 groups into contrapositions relative to one another (I).

With the objective of checking this hypothesis, syntheses were undertaken of a number of compounds with structure (I) and of some azo compounds [8] in which A_1 and A_2 are represented by CH_3, OCH_3 and OC_2H_5.**

*Auxochromic groups of the type of NH_2, OH, OR, etc. are chromophores of a special type (electron-donating chromophoric components A) on the bases of the character of their spectra and of a new and more rigid definition of the term "chromophore": "Chromophores are groups possessing electrons that participate in the absorption of light either independently or in conjunction with electrons of other chromophores" [5]. They introduce their p-electrons (p-π-conjugation) [7] into a cochromophore [5] (a complex chromophore in which the electronic systems of the chromophoric components are combined into a single, generalized electronic system) and thereby participate in the light absorption. Although CH_3 groups have a different mechanism of action (σ,π-conjugation) [7], they must be regarded as members of the A group [5].

**The work is a continuation of that commenced by V. I. Stavrovskaya [9, 10].

Compounds with 1 or 2 CH_3 groups are still colorless or nearly colorless (the donating properties of the CH_3 group are too weak). However compounds with one o-OCH_3 group (A_1) are lemon-yellow (Table 1 , nos. 1-3). The color deepens considerably after introduction of two OCH_3 and CH_3 or $(OCH_3)_2$ groups (nos. 4 and 5 are more deeply colored than nos. 1-3 in the crystal form). This is confirmed by the reflection spectra (Fig. 1). A marked intensification of color (change from light-yellow to orange) was also observed after introduction of two donor groups (I, $A_1 = OCH_3$ and $A_2 = CH_3$ or OCH_3) into a 4-benzamino derivative (I, $A_1 = A_2 = H$, $A_3 = NHCOCH_3$) (Nos. 6-9, Table 1). Figure 2 shows the reflection spectra of lemon-yellow No. 7(I, $A_1 = OCH_3$, $A_2 = H$, $A_3 = NHCOC_6H_5$) and orange No. 9 (I, $A_1 = A_2 = OCH_3$, $A_3 = NHCOC_6H_5$). Introduction of a second OCH_3 group is seen to intensify the color. Here again our ideas are confirmed.

The effect of two OCH_3 groups are found to be stronger in the absence of the $NHCOC_6H_5$ group (no. 5, $A_1 = A_2 = OC_2H_5$, $A_3 = H$, yellow-brown), whereas the additional presence of $A_3 = NHCOC_6H_5$ (no. 9) leads to an orange color (Fig. 2, curves 5 and 9). Again, compounds with two OC_2H_5 groups (no. 11, $A_1 = A_2 = OC_2H_5$, $A_3 = NHCOC_6H_5$) are only bright orange. Disturbance of the coplanarity may here be involved since the group C_6H_5CONH- probably has the structure $C_6H_5C(OH)=N-$.

Visual observations and reflection spectra consequently confirm the deepening of color on introduction of a second CH_3 or OCH_3 group (an electron donor) into an anilide residue in the para-position to the first OCH_3 group when compared with derivatives containing only one OCH_3 group. It should be noted that in presence of $A_1 = CH_3$ the introduction of a second $A_2 = CH_3$ or OCH_3 did not give the same effect as in the presence of $A_1 = OCH_3$ (nos. 12 and 13).

TABLE 1

Color of 4-Nitrobenzanilide Derivatives with the Structure of (I)

Prep. No.	A_1	A_2	A_3	Melting point	Color of crystal *	Molecular formula	N (in %) calc.	N (in %) found
1	CH_3	H	H	150°	Colorless	—	—	[9]
2	CH_3	CH_3	H	150.5—151	Off-white	$C_{15}H_{14}O_3N_2$	10.37	10.34 [9]
3	OCH_3	H	H	143	Lemon--yellow	—	—	[9]
4	OCH_3	CH_3	H	160	Deep-yellow	$C_{15}H_{14}O_3N_2$	9.79	9.79 [9]
5	OCH_3	OCH_3	H	180.5	Yellowish--brown	$C_{15}H_{14}O_5N_2$	9.28	9.56
6	H	H	NHCOPh	>300	Light-yellow	--	—	—
7	OCH_3	H	NHCOPh	269	Lemon--yellow	—	—	[9]
8	OCH_3	CH_3	NHCOPh	276.5	Deep-yellow	$C_{22}H_{19}O_5N_3$	10.37	10.63
9	OCH_3	OCH_3	NHCOPh	234	Orange	$C_{22}H_{19}O_6N_3$	9.95	10.15
10	OC_2H_5	OC_2H_5	NHCOPh	239—240	Deep-orange	$C_{24}H_{23}O_6N_3$	9.36	9.33
11	CH_3	CH_3	NHCOPh	275 [9]	Pale-yellow	$C_{23}H_{19}O_6N_3$	10.80	10.85 [9]
12	CH_3	OCH_3	NHCOPh	286 [9]	Light-orange	$C_{22}H_{19}O_5N_3$	10.37	10.32 [9]
13	H	OCH_3	NHCOPh	269 [9]	Yellowish	—	—	—

*In powder form the color is approximately the same; no. 5 is an exception (orange in powder form).

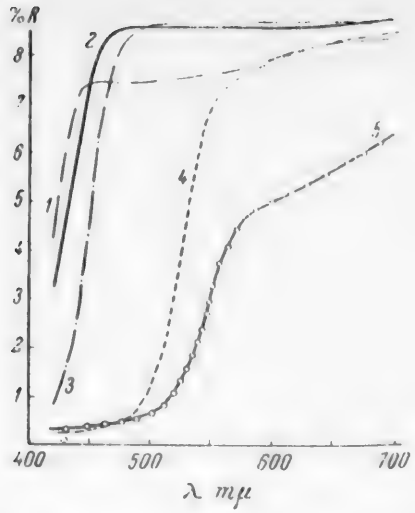


Fig. 1. Reflection spectra of derivatives of 4'-nitrobenzanilide (I). Curve numbers correspond to the numbers of the preparations in Table 1. 1) 2-CH_3, 2) 2,5-$(CH_3)_2$, 3) 2-OCH_3, 4) 2-OCH_3, 5-CH_3, 5) 2,5-$(OCH_3)_2$.

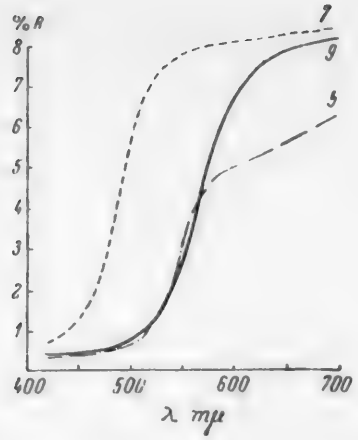
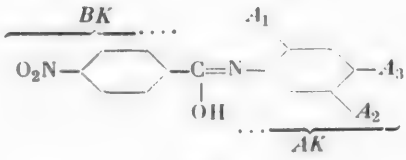


Fig. 2. Reflection spectra of derivatives of 4'-nitro-4-benzaminobenzaniline. Numbers correspond to those in Table 1. 5) 2,5-$(OCH_3)_2$, 7) 2-OCH_3, 4-NHCOPh 9) 2,5-$(OCH_3)_2$, 4-NHCOPh.

The color of compounds in the crystalline state is mainly associated with exomolecular interactions [4b] of the systems AK and BK (I). Taking into account a number of facts pointing to an imidol structure of the CONH group [1, 2],* we should expect also direct endomolecular interaction between the systems AK and BK across the double bond of the $-C(OH)=N-$group (IV).



(IV)

This expectation is confirmed by examination of the spectra of compounds in solution in alcohol (Table 2, Fig. 3). In presence of a first CH_3 group (A_1) the influence of a second CH_3 group in the 5-position (A_2) (no. 2) in solution is still negligible, just as it is in the crystalline state. Curves 1 and 2 nearly coincide (Fig. 3). Replacement of CH_3 (A_1) by OCH_3 (A_1) (no. 3) excites a bathochromic effect in the absorption spectrum with sharp shifting of the absorption limit** in solution. The effect is represented by a value of $\Delta\lambda$ 40 mμ at ϵ 2000 in comparison with no. 1 (curves 1 and 3 in Fig. 3 (see also Table 2)) and by the development of an inflection of about 290-300 mμ indicating the presence of band II. The whole of the curve in the 300-370 mμ region is located very much above the curve of compound no. 1.

In the region of the short-wave band I (β according to another system of nomenclature) the introduction of OCH_3 in place of CH_3 causes a slight hypsochromic shift of the maximum from 262 to 257 mμ ($\Delta\lambda = -5$) (curves 1 and 3 in Fig. 3, Table 2).

*One of the important facts confirming this structure of derivatives of 4-nitrobenzanilide (apart from the sharp bathochromic shift of the spectrum in comparison with nitrophenylacyl- and γ-(nitrophenyl)-butyryl-anilides) is the large hypsochromic shift of the spectrum of N-methyl derivatives of 4-nitrobenzanilide [2].

**Characterization of the spectrum by the magnitude of the shift of the absorption limit at ϵ = 1000 and 2000 was recommended [1] in the case of broad bands or sloping absorption curves without a well-defined maximum, as for example in the case of band I (β in another nomenclature) of compounds 3 to 5 (Fig. 3).

Comparison of nos. 3 and 4 shows that addition to $A_1 = OCH_3$ of a second donor group $A_2 = CH_3$ causes a bathochromic shift of the absorption boundary into the region above 350 mμ (Table 2, Fig. 3), while the intensity of absorption is weakened in the 305-320 mμ region. Still greater analogous shifts are observed on introduction of a second OCH_3 group (A_2) (no. 5). In addition to the bathochromic shift of the curve we observe here also an inflection which clearly points to the presence of a second absorption band II (α in another nomenclature) with a maximum at about 320-325 mμ. In presence of a first OCH_3 group (A_1) a slight bathochromic shift is also observed in the region of maximum I from 257 to 260 mμ, and the shift extends to 263 mμ on introduction of CH_3 and OCH_3 groups in A_2 (I).

TABLE 2

Effect of Introduction of CH_3 and OCH_3 Groups into Derivatives of 4-Nitrobenzanilide with $c = 10^{-4}$ in Alcohol

Preparation No.*	Formula (I)			Band I (β)		Band II (α)		Absorption boundary with ε equal to	
	A_1	A_2	A_3	λ_{max}	ε_{max}	λ_{max}	ε_{max}	2000	1000
1	CH_3	H	H	262	11950	None	—	328	348
2	CH_3	CH_3	H	260	11900	None	—	330	350
3	OCH_3	H	H	257	14100	~290—300	~7500	368	381
4	OCH_3	CH_3	H	260	12500	~290—300	~5500	374	392
5	OCH_3	OCH_3	H	263	12400	~320—325	~4500	384	402
14	H	H	OCH_3	256	18000	327	6020	386	404
15	H	H	OH	254	18000	335	5650	394	410
16	H	H	NMe_2	270	20800	380	4750	450	474

*Spectra of compounds 14-16 from data supplied to us by E. A. Smirnov [2].

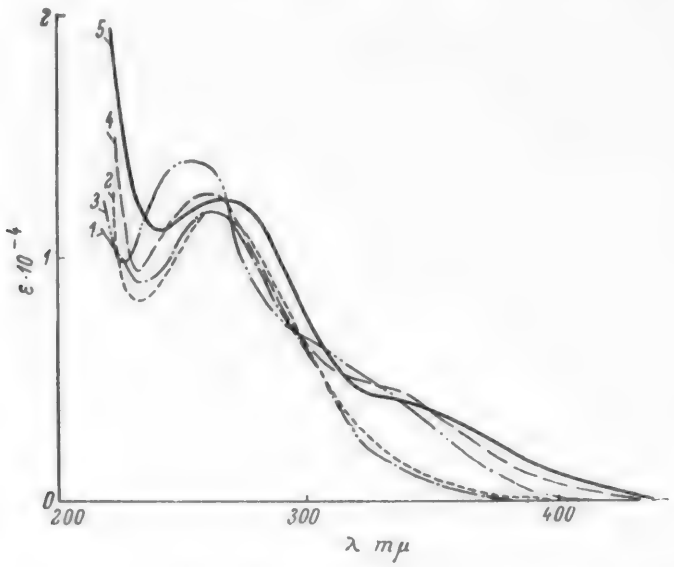


Fig. 3. Absorption spectra of derivatives of 4'-nitrobenzanilide (I). The numbers of the curves correspond to the numbers of compounds in Table 1. 1) 2-CH_3, 2) 2,5-$(CH_3)_2$, 3) 2-OCH_3, 4) 2-OCH_3, 5-CH_3, 5) 2,5-$(OCH_3)_2$.

Consequently the introduction of a second OCH_3 group and even of a CH_3 group into the para-position to the first donating OCH_3 group gave a definite bathochromic effect both in the solid state and in solution. The cause of this effect may possibly reside in the increased electronic shifts from AK to the BK side in the cochromophoric system (IV) due to enhancement of the donor properties of systems AK on introduction of an additional donor group in the contra-position [6]. This results, in accordance with the relation between the bathochromic effect and the degree of electronic shifts [5, 6], in a lowering of the energy of photoexcitation. In the region around 320-380 mμ the spectral curves of compounds 3, 4 and 5 possess the same characteristic inflection (Fig. 3) that we meet in the form of a band (band II) also in the spectra of compounds of structure (V) with OCH_3 (no. 14), OH (no. 15) and NMe_2 (no. 16).

The spectra of these compounds are compared in Fig. 4 (14, 15, 16, Table 2) using data kindly placed at our disposal by E. A. Smirnov [2]. The spectral curves of the p-methoxy (V, A = OCH_3) and p-hydroxy (V, A = OH) derivatives are very close together; band II in the case of p-OCH_3 has λ_{max} 327 mμ and ϵ_{max} 6020; in the case of p-OH we have λ_{max} 335 mμ and ε 5650. In the p-dimethylamino compound (V, A = NMe_2) both of the bands I and II are sharply displaced toward the longer waves: λ_{max} 380 mμ, ε 4750. It is interesting to note that whereas λ_{max} is shifted in the order OCH_3 < OH < NMe_2, the magnitudes of ϵ_{max} for band II fall in the order of OCH_3 > OH > NMe_2 (Table 2, 14 to 16).

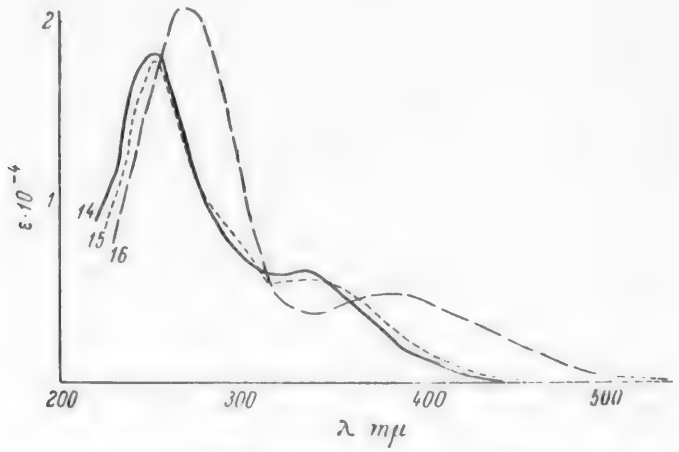
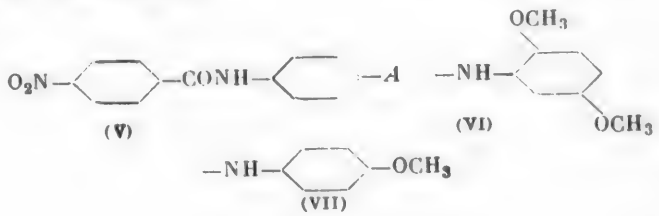


Fig. 4. Absorption spectra of derivatives of 4'-nitrobenzanilide (V) (Table 2). 14) 4-OCH_3; 15) 4-OH; 16) 4-NMe_2.

On comparing (Fig. 5) the spectra of 4' nitro-4-methoxybenzanilide (no. 14, (V), A = OCH_3) and 4'-nitro-2,5-dimethoxybenzanilide (no. 5, (I), $A_1 = A_2 = OCH_3$, A_3 = H) we see that band II of compound no. 5, which contains two donor OCH_3 groups in the contra-position (2,5-), is approximately in the same region as in the above nitrobenzoylarylamide which contains the donor OCH_3 group in the para-position to the NH group (no. 14, Fig. 5); in the 370-440 mμ region both of the branches of the curves coincide. This indicates that the donor system of (VI) with two additional donating OCH_3 groups in the contra-position (the second OCH_3 is in the para-position to the first OCH_3 and in the meta-position to the NH) has an effect very similar to that of the two-donor contra-system (VII) with one OCH_3 group in the para-position to the NH group. The effect of the single o-CH_3 group is considerably smaller (Fig. 5, nos. 3 and 5).



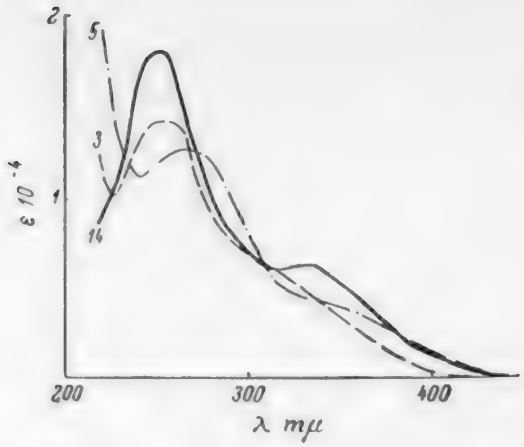


Fig. 5. Comparison of absorption spectra of derivatives of 4'-nitrobenzanilide (I) and (V) containing o-CH_3 groups. 3) 3-OCH_3, 5) 2,5-$(OCH_3)_2$, 14) 4-OCH_3.

EXPERIMENTAL

Compounds were prepared by the method of [1]. The numbers assigned to the preparations in the tables are the same as the numbers in the text. Color and melting point are listed in the table. Syntheses of the starting amines will be described in another communication.

1. 4'-Nitro-2-methylbenzanilide* [1-(4'-nitrobenzoylamino)-2-methylbenzene]. Readily soluble in alcohol, acetone, and benzene. It was purified by 3 boilings with alcohol.

2. 4'-Nitro-2,5-dimethylbenzanilide [1-(4'-nitrobenzoylamino)-2,5-dimethylbenzene]. Soluble in alcohol, acetone and benzene. It was purified from alcohol.

3. 4'-Nitro-2-methoxybenzanilide [1-(4'-nitrobenzoylamino)-2-methoxybenzene]. Readily soluble in alcohol, acetone and benzene It was thrice recrystallized from alcohol.

4. 4'-Nitro-2-methoxy-5-methylbenzanilide [1-(4'-nitrobenzoylamino)-2-methoxy-5-methylbenzene]. Prepared from 1-amino-2-methoxy-5-methylbenzene (cresidine). Poorly soluble in alcohol, acetone and benzene, better soluble in pyridine and chloroform. It was recrystallized from a large volume of alcohol.

5. 4'-Nitro-2,5-dimethoxybenzanilide [1-(4'-nitrobenzoylamino)-2,5-dimethoxybenzene]. Poorly soluble in alcohol, acetone, and benzene, more soluble in pyridine. Was recrystallized from a large volume of alcohol.

6. 6'-Nitro-4-benzoylaminobenzanilide [1-(4'-nitrobenzoylamino)-4-benzoylaminobenzene]. Prepared from 1-(4'-nitrobenzoylamino)-4-aminobenzene with m.p. 226-227°. Poorly soluble in alcohol, acetone, and benzene, better soluble in pyridine. Was recrystallized 3 times from pyridine.

7. 4'-Nitro-4-benzoylamino-2-methoxybenzanilide [1-(4'-nitrobenzoylamino)-4-benzoylamino-2-methoxybenzene]. Prepared from 1-amino-4-benzoylamino-2-methoxybenzene. Poorly soluble in alcohol, acetone, and benzene, better soluble in pyridine. Was purified by boiling in pyridine.

8. 4'-Nitro-4-nitrobenzoylamino-2-methoxy-2-methylbenzanilide [1-(4'-nitrobenzoylamino)-4-benzoylamino-2-methoxy-5-methylbenzene]. Prepared from 1-amino-4-benzoylamino-2-methoxy-5-methylbenzene. Poorly soluble in alcohol, benzene, and acetone, better soluble in pyridine. Purified by 3 boilings in a large volume of alcohol.

9. 4'-Nitro-4-benzanilide-2,5-dimethylbenzanilide [1-(4'-nitrobenzoylamino-4-benzoylamino)-2,5-dimethoxybenzene]. Prepared from the technical base (Fast Blue) of 1-amino-4-benzoylamino-2,5-dimethoxybenzene. Poorly soluble in alcohol, benzene, and acetone, more easily soluble in pyridine and chloroform. Was recrystallized from a large volume of alcohol.

10. 4'-Nitro-4-benzoylamino-2,5-diethoxybenzanilide [1-(4'-nitrobenzoylamino)-4-benzoylamino-2,5-diethoxybenzene]. Prepared from the technical base (Fast Blue BB) of 1-amino-4-benzoylamino-2,5-diethoxybenzene. Readily soluble in pyridine and chloroform, poorly soluble in alcohol, acetone, and benzene. Was recrystallized from a large volume of alcohol.

*The nitro- and diaminobenzanilides and their substituted derivatives have become important intermediates for synthesis of direct azo dyes. It is therefore desirable to simplify the nomenclature of these compounds and to regard them as derivatives of benzanilide, e.g., 4,4'-diaminobenzanilide (VIII) instead of 1-(4'-aminobenzoyl)-p-phenylenediamine or 1-(4'-aminobenzoylamino)-4-aminobenzene.

$H_2NC_6H_4CONHC_6H_4NH_2$
(VIII)

11. 4'-Nitro-4-benzoylamino-2,5-dimethylbenzanilide [1-(4'-nitrobenzoylamino)-2,5-dimethylbenzene]. Prepared from 1-amino-4-benzoylamino-2,5-dimethylbenzene. M.p. 179°. Poorly soluble in alcohol, benzene, ether, and acetone, readily soluble in pyridine. Purified by 3 boilings in alcohol.

12. 4'-Nitro-4-benzoylamino-2-methyl-5-methoxybenzanilide [1-(4'-nitrobenzoylamino)-2-methyl-5-methoxybenzene] [9]. Prepared from 1-amino 4-benzoylamino-2-methyl-5-methoxybenzene. M.p. 175°. Poorly soluble in alcohol, acetone, and benzene, more soluble in pyridine Was recrystallized from pyridine. Small, elongated needles, which formed a felted mass.

13. 4'-Nitro-4-benzoylamino-2-methoxybenzanilide [1-(4'-nitrobenzoylamino)-2-methoxybenzene]. Prepared from 1-amino-4-benzoylamino-5-methoxybenzene. Poorly soluble in alcohol, acetone, and benzene, more readily soluble in pyridine.

The absorption and reflection spectra were obtained with a Beckmann spectrophotometer. The reflection spectra were measured for substances rubbed in the form of fine powder onto Whatman paper.

SUMMARY

1. Two electron-donating groups in the para-position to one another create a contrapolarized system (AK) with enhanced electron-donating ability which leads to deepening of the color. With the objective of studying the effect on the reflection and absorption spectra of the addition of two electron-donating groups in the contra-position, an investigation was undertaken of 4-nitrobenzoylarylamides with structure (I) containing additional electron-donating CH_3, OCH_3, and OC_2H_5 groups in the anilide ring in the 2 and 5 positions.

2. Introduction of two CH_3 groups has a negligible effect, but the addition to the 2-methoxy derivative of a second donating 5-CH_3 group and especially of the 5-OCH_3 group already leads to a strong bathochromic shift of the reflection and absorption spectra toward the long-wave side. In the case of 4'-nitro-2,5-dimethoxybenzanilide a pronounced shelf appears which points to the development of an absorption band II (λ_{max} 320-355 mμ).

3. Comparison of the spectrum of the 2,5-dimethoxy derivative (no. 5) with the absorption spectra of 4-nitrobenzoylanilides with a second donor group (OCH_3, OH, NMe_2) in the para-position to the NH group shows that the effect of the 2,5-dimethoxy 2-donor system [1-CONH, 2,5-$(OCH_3)_2$] is extremely similar to that of the 4-methoxy group [1-CONH, 4-OCH_3].

4. In presence of a 4-benzamino group the influence on the solid-state color of two donor groups is likewise very marked and leads to deepening of the color from bright yellow to bright orange in the order 2-OCH_3 < < 5-CH_3 < 2,5-$(OCH_3)_2$ < 2,5-(OC_2H_5).

The spectrum in solution is governed by the interaction of the systems AK and BK across the double bond of the iminol group (IV), whereas the color and the reflection spectrum in the crystalline solid state are also associated with exomolecular interactions.

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CONTRAPOLARIZED SYSTEMS AND COLOR

II. REFLECTION SPECTRA OF DERIVATIVES OF N-[β-(4-NITROPHENYL)-ETHYL]-ANILINE WITH DONOR CHROMOPHORES IN THE PARA- AND META-POSITIONS*

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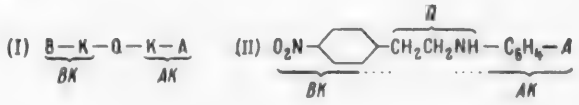
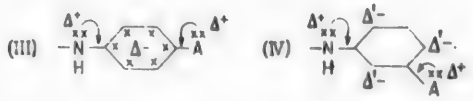
Moscow Potemkin Institute of Education

1. We have investigated compounds of the type of (II) – derivatives of N-[β-(4-nitrophenyl)-ethyl]-aniline with Q = $-CH_2CH_2NH-$ in connection with a study of componnds containing nonadjacent chromophoric systems with structure (I) [1, 2].



Here BK is a complex electronophilic chromophoric system (B is an electronophilic chromophore – NO_2 in the present case), K is the conjugated chromophoric system of benzene, AK is a complex electron-donating system (A is an electron-donating chromophore)** [1, 3]. BK and AK are separated by group Q which interrupts the conjugation. The influence of the following groups of type A was studied: CH_3, OCH_3, OH, $NHCOCH_3$, NH_2 in the para- and meta-position to the first donor-chromophore NH entering into the composition of Q***

The color of compounds of this type in crystals is bound up with the exomolecular interaction [2] of system AK with system BK (II). The purpose of the present investigation was to investigate the differing degrees of influence of A in the para- and meta-positions to the NH group. When A is in the para-position a two-donor contrapolarized system AKA (III) is created. In such contrasystems the structure is governed by the opposing influences of the two donors (hence the prefix contra) on the π-system of the benzene ring [1, 3, 5, 9, 10].



*The work is a continuation of the investigation started by Z. M. Bairamov [4] and links up with the investigations of derivatives of 4-nitro- and 2,4-dinitrobenzanilides by V. I. Stavrovskaya [5, 6] and E. A. Smirnov [7] and of derivatives of nitrobenzylaminostilbene by P. I. Samokish [8, 2].

**Groups of the type of A (NH_2, OH, OR, etc.) are chromophores by virtue of the character of their spectra and in the light of a new and more rigorous definition of the term "chromophore:" "Chromophores are groups possessing electrons that participate in light absorption independently or in conjunction with electrons of other chromophores" [3].

***If we assume that the NH group is the first donating chromophore and group A is the second, then the general scheme (I) of the structure of type (II) molecules can be more specifically represented by $B-K-Q-A^1-K-A^2$ [1].

In previous investigations it was concluded that this leads to diminution of the total electron-donating ability of the system AK, and to intensification of its reactivity with electronophilic systems BK due to the creation of a stronger electron-donating center Δ^- in (III).

If A is in the meta-position (IV), a syn-polarized system (with the donor groups exerting identical effects) is created. In this system the three electron-donating centers Δ'^- are weaker than Δ^- in the system (III): $\Delta^- > \Delta'^-$. Consequently with A in the para-position we should expect to observe stronger bathochromic effects than when A is in the meta-position (for a given structure of A) both in the solid (crystalline) state and in fairly strongly concentrated solutions in which exomolecular interactions can be developed.

The table gives the colors of the compounds that we synthesized and some quantitative data for the reflection spectra (% R for some wavelengths, λ in mμ).

Comparison of Colors of Compounds with the Structure $RCH_2CH_2NHC_6H_4A$ where R = = p-$O_2NC_6H_4$*

Prep. No.	Formula	Color of substance		Reflection spectra (% R for λ in mμ)				
		in crystals	in powder	400	450	500	600	700
1	$RCH_2CH_2NHC_6H_5$	Yellow	Pale-yellow	8.4	26.0	71.0	84.4	85.3
2	$RCH_2CH_2NHC_6H_4CH_3$-p	Yellow	Pale-yellow	12.5	39.5	68.0	81.0	82.8
3a	$RCH_2CH_2NHC_6H_4OCH_3$-p	Orange-red	Orange	8.0	12.0	26.8	72.8	81.5
3b	The same**	Light-orange	Yellow-orange	19.5	28.5	48.5	77.0	81.0
4a	$RCH_2CH_2NHC_6H_4OH$-p	Red	Light-brown	6.0	8.5	17.0	55.0	78.0
4b	The same***	Golden-orange	Yellow-orange	11.5	15.0	26.5	63.5	79.0
5	$R(CH_2)_2NHC_6H_4NHCOCH_3$-p	Orange with tinge of brown	Light-orange	9.2	12.0	23.5	70.0	80.0
6	$RCH_2CH_2NHC_6H_4NH_2$-p	Dark-red	Brown	8.0	7.6	9.2	32.7	71.0
7	$RCH_2CH_2NHC_6H_4OCH_3$-m	Brown-yellow	Yellow	6.0	23.2	56.0	70.0	75.5
8	$RCH_2CH_2NHC_6H_4OH$-m	Light-brown	Brownish-yellow	6.5	7.5	20.0	56.0	71.0
9	$RCH_2CH_2NHC_6H_4NHCOCH_3$-m	Light-orange	Light-orange	8.4	10.0	24.0	71.5	80.0
10	$RCH_2CH_2NHC_6H_4NH_2$-m	Yellow-green	Yellow-brown	7.5	18.5	44.5	65.5	72.5

* All of the compounds were recrystallized from alcohol unless otherwise stated.
** From gasoline-ligroine mixture.
*** From toluene-gasoline mixture.

2. Effect of A in the para-position to the NH group. Introduction of a second donor in the para-position to the NH group results in deepening of color. This effect is intensified with intensification of the donor properties of the second donor group: H < CH_3 < OCH_3 < $NHCOCH_3$ < OH < NH_2.* It must be remembered that the color in the solid crystalline state is complicated by the well-marked phenomena of chromoisomerism.** It is therefore necessary to compare the more deeply colored forms obtained by crystallization from the same solvent. The preparations were recrystallized from alcohol. The color was considerably intensified after the substances had been recrystallized from nonpolar solvents. Prep. 3a (see table) formed orange-red needles from alcohol but crystallized with a light-orange color from a mixture of gasoline and ligroine (3b). Compound 4a is dark-red after crystallization from chloroform; when purified in a chromatographic column (from alcohol) it forms red

* The anomalous position of p-OH is discussed later.

needles, while treatment with gasoline-toluene mixture under the same conditions gives gold-to-orange plates (4b). The shape of the crystals also changed. The melting points of the different forms are identical. The chromoisomerism of compounds of this type merits further study. X-ray structural analysis should be used to establish the differences in packing of the crystals of the different forms. The influence of the p-CH_3 group is still negligible. Both of the compounds 1 and 2 are nearly identical in color. The curves of the reflection spectra intersect in such a manner,(Fig. 1, curves 1 and 2) that in the 500-650 mμ region the compound with the p-CH_3 group absorbs more strongly, whereas in the 400-500 mμ region the branch of the curve with the p-CH_3 group unexpectedly undergoes hypsochromic displacement and the intensity of absorption in the region of the maximum at 400 mμ falls (% R 12.5 instead of 8.4). A possible cause of this could be the presence in compound 2 of another, less deeply colored, chromoisomeric form. Conversely, compound 1 might contain a more deeply colored form.

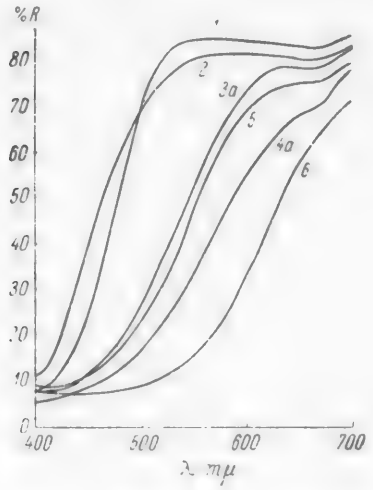


Fig. 1. Influence on the reflection spectrum of a second electron-donating group A (II) in the para-position to the NH group. 1) A = H; 2) A = = p-CH_3; 3a) A = p-OCH_3; 4a) A = p-OH; 5) A = p-$NHCOCH_3$; 6) A = p-NH_2.

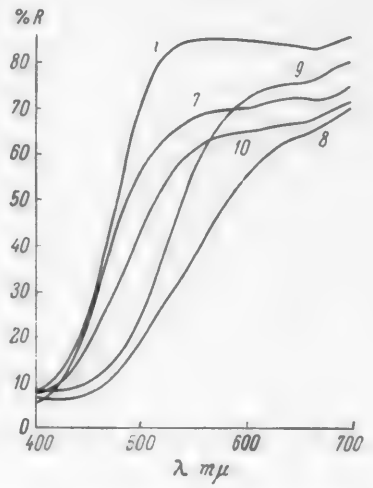


Fig. 2. Influence on the reflection spectrum of a second electron-donating group A (II) in the meta-position to the hydrogen. 1) A = H; 7) A = m-OCH_3; 8) A = m-OH; 9) A = m-$NHCOCH_3$; 10) A = m-NH_2.

The introduction of a p-OCH_3 (3a) and p-$NHCOCH_3$ group (5) has a much greater effect than the introduction of a p-CH_3 group. The curves of the reflection spectra of compounds containing p-OCH_3 and p-$NHCOCH_3$ groups are extremely close to one another (Fig. 1), but the curve of the p-acetamino compound is shifted to the long-wave side and follows a lower course throughout, due to the stronger donor properties of the $NHCOCH_3$ group in comparison with the OCH_3 group.

The color of compound 4a (containing p-OH) is unexpectedly deep (Fig. 1). Whereas normally the OCH_3 and OH have very similar effects on color and spectra, in our case the compound with p-OH had a considerably deeper color – dark-red (from chloroform) – than the compound containing p-OCH_3 (3a) and p-$NHCOCH_3$ (5). Such a deep color of N-[β-(4-nitrophenyl)-ethyl]-p- aminophenol could be due to contamination by oxidation products during synthesis. Compound 4a was therefore subjected to further purification in a chromatographic column with Al_2O_3 and thereupon recrystallized from alcohol. Red needles (4a) were obtained. The second modification – gold-to-orange plates (4b) – was obtained by recrystallization from a mixture of toluene and gasoline. Although the curve of the reflection spectrum was displaced in the direction of intensified color after purification, the first modification of compound (4a) with p-OH has a very much deeper color than the compound with p-OCH_3 (3a).

As has been expected, the compound with a p-NH_2 group (6) had the deepest color (dark-red). Color and melting point did not alter after purification in a chromatographic column. A compound with a p-NMe_2 group was not obtained due to the ease of formation of secondary oxidation products during synthesis.

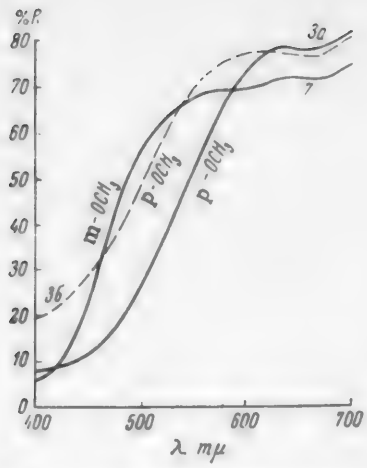


Fig. 3. Comparison of reflection spectra of compounds (II): two forms with A = p-OCH_3 and a compound with A = m-OCH_3.

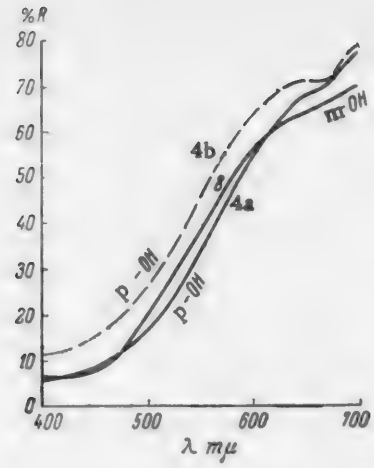


Fig. 4. Comparison of reflection spectra of compounds (II): two forms with A = = p-OH and a compound with A = m-OH.

3. Influence of A in the meta-position to the NH group. Many unexpected features have been observed in the color and reflection spectra of meta-substituted derivatives. The introduction of donor groups in the meta-position likewise caused a bathochromic shift in relation to the unsubstituted compound, but the relative order of the curves of the reflection spectra diverged from the order of the shifts observed for para-isomers: in the 400-550 mμ region: H < OCH_3 < NH_2 < $NHCOCH_3$ < OH; in the 550-700 mμ region: H < $NHCOCH_3$ < OCH_3 < NH_2 < OH (Fig. 2). Introduction of m-OCH_3 (brownish-yellow, 7) caused a bathochromic shift of the curve of the reflection spectrum in comparison with compound 1 which does not contain A. A considerably greater bathochromic shift is observed for m-$NHCOCH_3$ (1, light-orange). Consequently the introduction of electron-donating chromophores m-OCH_3 and m-$NHCOCH_3$ resulted in a bathochromic shift in relation to the unsubstituted compound. But the effect of m-OCH_3 was very much weaker than that of p-OCH_3: transfer of OCH_3 from the para- to the meta-position is associated with a strong hypsochromic shift of color (3a, 7, Fig. 3). It is interesting that in the 400 mμ region the meta-isomer possesses rather stronger absorption. The compound containing m-$NHCOCH_3$ has a deeper color than the compound with m-OCH_3 (the same order as in the case of the para-isomers is found). An unexpected feature is the close proximity of the reflection spectra of compounds with p- and m-$NHCOCH_3$ (5, 9, Fig. 5), although here also the curve of the meta-isomer in the 400-600 mμ region undergoes a hypsochromic shift in relation to the para-isomer. Just as in the case of the para-isomer, the color of the compound containing an m-OH group (8) is unexpectedly deep: its reflection spectrum is very much more bathochromically shifted than that of the remaining meta-isomers. Here also, however, the curve of the meta-derivative undergoes a hypsochromic shift, although very much smaller than that of the para-derivative (4a, 8, Fig. 4).

Also unexpected is the position of the curve of the m-NH_2 compound (10); it is less deeply colored than the compound with m-$NHCOCH_3$ and m-OH. In the 400-550 mμ region the reflection curve of this compound is even more hypsochromic in relation to the compound with m-$NHCOCH_3$, but in the 550-700 mμ region we observe a considerably stronger absorption (8, 9, 10, Fig. 2). Due to the slight deepening of color on introduction of an NH_2 group into the meta-position, there is a sharp bathochromic shift when the NH_2 group is transferred from the meta- to the para-position (6, 10, Fig. 6). The investigations therefore confirm that two-donor systems with a meta-position A are weaker electron-donating systems than the corresponding two-donor contrapolarized systems with a para-position A. The unexpected deviations of the meta-derivatives from the order, color and position of the curves of the reflection spectra of the para-derivatives are possibly associated with steric influences on the packing arrangement of molecules in the crystal and on the interaction of systems AK and BK in the solid state. We may proceed to evaluate the phenomena which have been described after we have measured the absorption spectra and carried out an x-ray analysis of the crystal lattice.

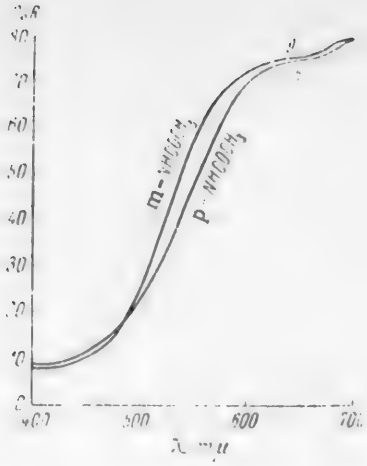


Fig. 5. Comparison of reflection spectra of compounds (II) with A = p- and m-$NHCOCH_3$.

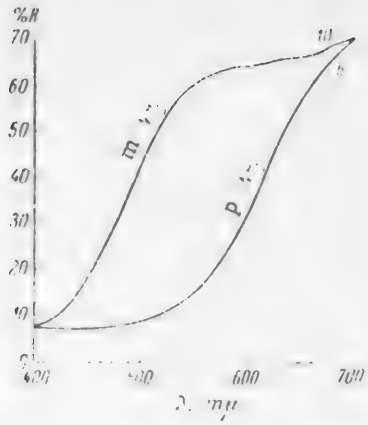


Fig. 6. Comparison of the reflection spectra of compounds (II) with A = p- and m-NH_2.

EXPERIMENTAL

β-Phenylethyl chloride. The method of Bernajes and Herrara [11] was slightly modified: the quantity of toluene was reduced, the initial reaction temperature was raised to 0 to 5° (from −5°) and the excess of thionyl chloride was increased; after the whole of the thionyl chloride had been added, the reaction mass was stirred 5 hours at room temperature.

To 200 g β-phenylethyl alcohol and 340 ml toluene at 0° (or not higher than 5°), with mechanical stirring, was added dropwise 260 g thionyl chloride (i.e., 1.3 times the quantity of β-phenylethyl alcohol) in the course of 2-2.5 hours. After the thionyl chloride had been added, the mass was held 5 hours at room temperature. The excess of thionyl chloride and the toluene were distilled off, and then the β-phenylethyl chloride was distilled in vacuo; b.p. 91-92° at 20 mm. Yield 208 g (90 to 95%).

β-(4-Nitrophenyl)-ethyl chloride (NPC). The procedure was based on that for the preparation of β-(4-nitrophenyl)-ethyl bromide [12] but the reaction was performed at a higher temperature. In the course of 0.4 hours 152.5 g nitric acid (d 1.6) was added, with mechanical stirring and cooling to 0°, to a mixture of 247 g acetic anhydride and 145 g acetic acid. Thereupon 140.5 g β-phenylethyl chloride was stirred in from a separating funnel in the course of 3.5 hours. During this operation the temperature of the reaction mass was not allowed to rise above 15°. After 5-hours' stirring at room temperature, the reaction mass was run into a suspension (cooled to 0°) of 250 g sodium carbonate in 1 liter water and left overnight. The crude β-(4-nitrophenyl)-ethyl chloride was extracted with benzene. The benzene extract was washed to neutrality with water, then with sodium carbonate solution and again with water. The benzene was taken off at first at atmospheric pressure and later in vacuo until the pressure did not reach 10 mm during heating of the flask on a boiling water bath. The residue of brown oil was run in the hot state into a beaker; on cooling it deposited yellow-orange crystals. They were filtered and recrystallized from methanol. Light-yellow needles with m.p. 49°. Yield 79 g (36 to 40%).

1. N-[β-(4-Nitrophenyl)-ethyl]-aniline. Heating of NPC with aniline at 140° [4] gives a large amount of resins and a dialkyl derivative. In view of the accelerating effect of alcohols on the reaction of amines with alkyl halides [13] we tried out alcohols as reaction media. The use of isoamyl alcohol (b.p. 130°) protects the reaction mixture against overheating and gives a pure product in higher yield. 7 g (1 mole) NPC and 7.5 g (4 moles) aniline were heated in 40 ml isoamyl alcohol for 18 hours at the boil. After cooling, a little concentrated hydrochloric acid was added to the reaction mixture. A white precipitate of hydrochlorides settled to the bottom of the beaker after a short time. The precipitate was filtered and washed with water, after which bicarbonate was added to separate the amine. The yellow precipitate was filtered and crystallized from methanol. Almost at once the hot solution deposited the more difficultly soluble bis-N,N-[β-(4-nitrophenyl)-ethyl]-aniline; the light-yellow crystals were separated by decantation and recrystallized from benzene; m.p. 171° [4], yield

0.5 g. The alcoholic mother liquor, decanted off, deposited bright-yellow needles of N-[β-(4-nitrophenyl)-ethyl]-aniline on standing. Two recrystallizations from methanol gave 2 g (18%), m.p. 69° [4]. The compounds described below were obtained by similar means unless otherwise stated.

2. N-[β-(4-Nitrophenyl)-ethyl]-p-toluidine. From 7 g (1 mole) NPC and 16 g (3 moles) p-toluidine was obtained 7.8 g (60%). Yellow plates from alcohol, m.p. 79°.

Found %: N 11.21 $C_{15}H_{16}O_2N_2$. Calculated %: N 10.93.

3. N-[β-(4-Nitrophenyl)-ethyl]-p-anisidine. Obtained in two forms. Red-orange needles, m.p. 91°, from alcohol. Yield 7.5 g (35%).

Found %: N 10.51. $C_{15}H_{16}O_2N_2$. Calculated %: N 10.28.

From a mixture of gasoline and ligroine the product crystallized as yellow-orange needles, m.p. 91°.

4. N-[β-(4-Nitrophenyl)-ethyl]-p-aminophenol. The boiling period was shortened to 12.5 hr. After the reaction, the isoamyl alcohol was driven off with steam. Subsequent procedure was as before. Dark-red needles from chloroform. Yield 2.6 g (34%). Further purification in a chromatographic column was effected to eliminate possible contamination with products of oxidation. The following two modifications were obtained in similar fashion to the benzyl derivative [14]: 1) red plates from alcohol, m.p. 137°; 2) golden-orange plates from toluene-gasoline, m.p. 137-138°.

Analysis of red form: Found %: N 11.11. $C_{14}H_{14}O_3N_2$. Calculated %: N 10.85.

5. N-[β-(4-Nitrophenyl)-ethyl]-p-aminoacetanilide. Orange needles from alcohol, m.p. 164°. Yield 4.25 g (30%).

Found %: N 14.42. $C_{16}H_{17}O_3N_3$. Calculated %: N 14.34.

6. N-[β-(4-Nitrophenyl)-ethyl]-p-phenylenediamine. Prepared by hydrolysis of product 5. 1 g of product 5 was boiled with 20 ml 20% hydrochloric acid for 3 hours. The precipitated hydrochloride was filtered, dissolved in excess water and neutralized with sodium carbonate. The resulting dark-red precipitate was filtered and recrystallized from alcohol. Dark-red needles, m.p. 128°. Yield nearly quantitative. Treatment in a chromatographic column did not alter the color or melting point.

Found %: N 16.21. $C_{14}H_{15}O_2N_3$. Calculated %: N 16.33.

7. N-[β-(4-Nitrophenyl)-ethyl]-m-anisidine. A mixture of 5.6 g (1 mole) NPC and 12.5 g (2 moles) m-anisidine was boiled 18 hours in a medium of isoamyl alcohol. A thick brown oil remained after the isoamyl alcohol had been distilled off in steam. The oil was dissolved in alcohol and the solution poured into excess water. After a short time light-brown crystals separated on the walls of the vessel. They were filtered and twice recrystallized from dilute alcohol in presence of carbon. Dark-yellow needles with a greenish tinge. Yield 3.3 g (30%), m.p. 85°.

Found %: N 10.37. $C_{15}H_{16}O_3N_2$. Calculated %: N 10.29.

8. N-[β-(4-Nitrophenyl)-ethyl]-m-aminophenol. Preparation on the same lines as that of the p-aminophenol derivative. Ths viscous, brownish paste was treated with 10% hydrochloric acid solution and then heated nearly to the boil with excess of water in order to remove unreacted m-aminophenol. It was recrystallized from dilute alcohol containing carbon. Light-brown needles, m.p. 189-190° (decomp.).

Found %: N 10.93. $C_{14}H_{14}O_3N_2$. Calculated %: N 10.85.

9. N-[β-(4-Nitrophenyl)-ethyl]-m-aminoacetanilide. Prepared on the same lines as preparation 7. It was crystallized from dilute alcohol. Yield 2.1 g (15%). Light-orange prisms, m.p. 136-137°.

Found %: N 14.23. $C_{16}H_{17}O_3N_3$. Calculated %: N 14.34.

10. N-[β-(4-Nitrophenyl)-ethyl]-m-phenylenediamine. Prepared on the same lines as preparation 9. It was recrystallized from dilute alcohol; greenish-yellow needles with m.p. 95°. Yield nearly quantitative.

Found %: N 16.23. $C_{14}H_{15}O_2N_3$. Calculated %: N 16.33.

Reflection spectra in the 400- to 700 mμ region were obtained with the help of the Hardy recording spectrophotometer. The finely pulverized preparation was spread on semi-Whatman paper. Measurements were made on the percentage light reflection by the surface of the powder spread on the paper as compared with the light reflection by a surface of compressed magnesia powder whose reflection was taken as 100%.

SUMMARY

1. A series of derivatives of N-[β-(4-nitrophenyl)-ethyl]-aniline of the general formula (II) where synthesized; A is one of the electron-donating groups CH_3, OCH_3, OH, $NHCOCH_3$ in the para- or meta-position to the NH group. All of the synthesized compounds were colored in spite of the presence in the conjugation-interrupting group Q of two CH_2 groups so that the existence of a continuously conjugated chain is excluded. The most deeply colored compound, containing a p-NH_2 group, has a dark-red color.

2. The regularities of the changes of color of the compounds that were observed visually were given added precision with the help of the reflection spectra of the pulverized substances.

3. The main cause of the coloration of the compounds in question in the solid state must be sought in the direct interaction of the electronophilic (BK) and electron-donating (AK) complex systems through exomolecular forces, i.e., the forces governing the formation of complex compounds of nitro bodies with aromatic amines and phenols.

4. The investigation showed that introduction of a donor group in the para-position intensifies the color to a greater extent than its introduction in the meta-position: a para-two-donor contrapolarized system is a stronger donor than a meta-two-donor syn-polarized system.

In the case of a para-compound the order of deepening of color is the same as the order determined by the strength of the electron-donating chromophore. An anomaly is the unexpectedly deep color of the para-hydroxy derivative. The OH group also had an unusually powerful effect in the meta-position. Compounds of the meta-series exhibited unexpected differences, in respect to the sequence of influence of the groups, compared with the sequence in the para-compounds. An explanation is required, for example, of the unexpectedly weak effect of the m-NH_2 group.

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UNSATURATED HYDROCARBONS

VII. THE SYNTHESIS OF p-METHYLDIPHENYL

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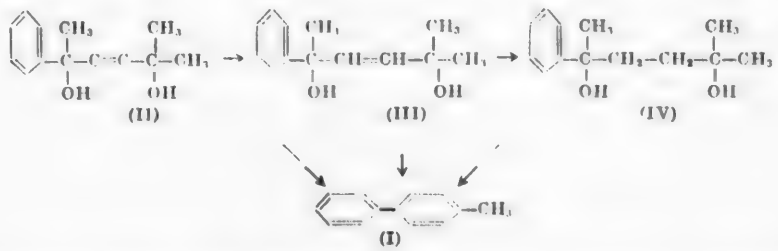
Patents [1] and journal articles [2] have described the catalytic aromatization of divinylacetylenic compounds and of the products of their partial hydrogenation as a method of preparation of aromatic hydrocarbons of a given structure. It was of interest to study the possibility of extending this reaction to the preparation of polyphenyl systems – hydrocarbons of the diphenyl, terphenyl, etc. systems. In the first instance we undertook the synthesis of p-methyldiphenyl.

Several cases of aromatization of alkaryl compounds are described in the literature [3]. No study appears to have been made, however, of the catalytic aromatization of alkyl- or alkenylbenzenes containing a side chain sufficiently long to afford the possibility of closure of a second six-membered ring. However certain reactions of cyclization, cyclodehydration and the like are known to proceed by a somewhat similar mechanism and to lead to products identical with, or similar to, those resulting from catalytic aromatization [4].

Special interest is attached to a paper [5] on the cyclization of 2-methyl-5-phenyl-2,5-hexanediol, which ought to give p-methyldiphenyl by our suggested mechanism. However, under the action of hydrogen fluoride or concentrated sulfuric acid this glycol gives a mixture of 1,1,4-trimethyltetralin and 1,2,4-trimethylnaphthalene. On the other hand, 1-phenyl-1,3,5-hexatriene, as well as the corresponding phenylhexadienic alcohols, are converted over Al_2O_3 into phenylcyclohexadiene [6]. Under the conditions of catalytic dehydrogenation the latter gives diphenyl. Over platinized carbon, phenylcycloheptane undergoes transformations that proceed with intermediate cleavage of the 7-membered ring and lead to a mixture of o-, m- and p-methyldiphenyls, diphenyl, and fluorene [7].

We propose the following route to the synthesis of p-methyldiphenyl (I): it involves aromatization of 2-methyl-5-phenyl-3-hexyne-2,5-diol (II) or of the products of its hydrogenation – 2-methyl-5-phenyl-3-hexen-2,5-diol (III) and 2-methyl-5-phenyl-2,5-hexanediol (IV).



Diol (II) can be easily prepared by the Grignard reaction [8] from 3-methyl-1-butyne-3-ol and acetophenone, or by the Favorskii reaction but in lower yield [9].

$$\left[C_6H_5-C(=CH_2)-C\equiv C-C(CH_3)=CH_2 \right]$$
(V)

Aromatization of diol (II) probably goes via the step of its dehydration to the corresponding divinylacetylenic hydrocarbon – 2-methyl-5-phenyl-1,5-hexadiene-3-yne (V) – since oxidic aromatization catalysts are also dehydration catalysts.* Aromatization was effected over $MgO-Cr_2O_3-Al_2O_3$ catalyst (2 : 18 : 80) at 380-510° and at various space velocities. Under the optimum conditions (430°, 0.28 kg/l·cat·hr) the yield of p-methyldiphenyl does not exceed 11-13%. As in previously described cases, we increased the yield by hydrogenating the starting diol (II) with one and two moles of hydrogen to give glycols (III) and (IV) respectively. Aromatization of glycol (III) under optimum conditions (482°, 0.36 kg/l·cat·hr) led to a yield of 42%; aromatization of glycol (IV) (550°, 0.66 kg/l·cat·hr) gave 46.5% yield.

The structure of the p-methyldiphenyl was confirmed by its oxidation with 2% potassium permanganate to p-phenylbenzoic acid whose constants agreed with those in the literature [7]. The ultraviolet absorption spectrum of (I) also corresponds to that described in the literature [11]. **

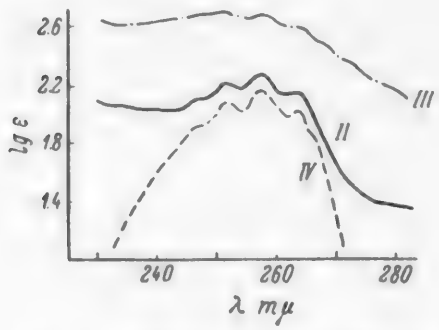


Fig. 1. Ultraviolet absorption spectra of glycols (II-IV) (solvent: ethanol).

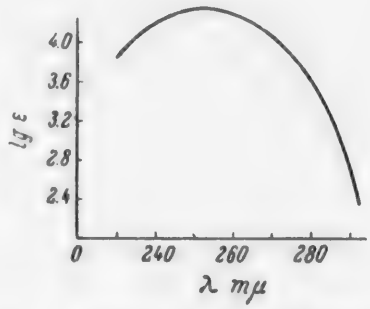


Fig. 2. Ultraviolet absorption spectrum of p-methyldiphenyl (solvent: ethanol).

An experiment in which diol (IV) was passed over quartz was carried out in order to clarify the nature of the reaction. The treatment did not yield any products with $n^{20}D$ greater than 1.5349. It was thereby demonstrated that the aromatization of glycols (II), (III) and (IV) is a catalytic reaction.

EXPERIMENTAL

2-Methyl-5-phenyl-3-hexyne-2,5-diol. 63 g dimethylethynylcarbinol [12] in 100 ml ether was added with cooling in the course of 50 minutes to an ethereal solution of C_2H_5MgBr (from 38 g magnesium and 173 g C_2H_5Br). The reaction mass was stirred at the boil for 45 minutes. It was then again cooled with ice and 71 g acetophenone in 100 ml ether was slowly added (2-3 hr). After standing for 3-4 days with periodic stirring, the product was decomposed with moist ether and water. The precipitate was dissolved in 5-10% H_2SO_4 and extracted. The ether was driven off in a nitrogen stream at a bath temperature not exceeding 60°. The residue quickly crystallized. It had m.p. 81-82° after recrystallization from ligroine. Literature data: m.p. 81.5-82° [8], 81° [9]. Yield 110 g (91%). The ultraviolet absorption spectra of (II), (III) and (IV) are shown in Fig. 1.

Hydrogenation of 2-methyl-5-phenyl-3-hexyne-2,5-diol. 1) 51 g of acetylenic glycol in 75 ml methanol was hydrogenated at room temperature in presence of $Pd/CaCO_3$ catalyst. After 0.25 mole hydrogen had been taken up, the palladium was filtered off, the methanol was taken off in vacuo, and the residue was distilled. There was obtained 41.6 g (80.7%) 2-methyl-5-phenyl-3-hexen-2,5-diol. A viscous liquid rapidly turning red in the air; b.p. 134-135° (4 mm), $n^{20}D$ 1.5240.

* We did not use hydrocarbon (V) as a starting substance because its preparation was hindered by its ease of polymerization [10].

** Spectra were plotted with the SF-4 spectrophotometer.

Aromatization of Glycols Over $MgO-Cr_2O_3-Al_2O_3$ (2 : 18 : 80)

Expt. temperature	Quantity of glycol passed in (g)	Feed rate (kcal/l. cat. hr)	Yield of crude p-methyldiphenyl (in g)
2-Methyl-5-phenyl-2,5-hexanediol			
412	6.6	0.21	1.32
485	8.9	0.21	2.08
512	9	0.22	3.43
510	9	0.2	3.41
510	9	0.47	3.81
535	9.2	0.46	4.17
555	9.2	0.47	3.54
555	9	0.67	4.73
555	18	0.66	9.65
555	9	0.70	4.21
570	8.8	0.65	3.81
534	9.1	0.61	3.87
510	9	0.67	3.36
2-Methyl-5-phenyl-3-hexen-2,5-diol			
460	8.9	0.36	3.88
482	8.4	0.36	4.07
480	9.3	0.24	3.28
482	8.45	0.51	4.04
512	9.45	0.38	4.12
520	9	0.55	3.53
2-Methyl-5-phenyl-3-hexyne-2,5-diol			
412	9	0.196	1.22
412	9	0.262	1.58
415	9	0.368	1.14
430	9	0.278	1.58
430	9	0.365	1.43
450	9	0.287	1.36
450	9	0.365	1.51
452	8.7	0.483	0.6

Found %: C 76.17; H 8.68. $C_{13}H_{18}O_2$. Calculated %: C 75.67; H 8.79.

2) 169.5 g diol in 150 ml methanol was hydrogenated over skeletal nickel catalyst at room temperature and with an initial hydrogen pressure of 150 atm until hydrogen ceased to be absorbed. Yield of 2-methyl-5-phenylhexane-2,5-diol, 160.31 g (92.7%).

B.p. 148-150° (4 mm), m.p. 72-73° (from ligroine). Literature data [5]: m.p. 74-75°.

Found %: C 75.15; H 9.75. $C_{13}H_{20}O_2$. Calculated %: C 74.94; H 9.68.

Aromatization of glycols. Aromatization of 2-methyl-5-phenyl-2,5-hexanediol was effected over $MgO-Cr_2O_3-Al_2O_3$ (2 : 18 : 80) catalyst [2]. A quartz tube (950 × 19 mm) was placed in a tubular furnace. The temperature was regulated to within 2°. A thermocouple was inserted in the catalyst bed (length of bed 90 cm). The glycol was admitted in the form of a 20% solution in benzene from a proportioning device with an electrolyzer [2]. Before and after the experiment the system was purged with nitrogen. Contact of the first portions of substance with the catalyst was marked by spontaneous rise of temperature by 20-30°. The temperature then fell to the required level in 5-10 minutes. The catalyst was regenerated by air-blowing for 2.5 hours at 500-600°. A special experiment established that benzene only reacts to an insignificant extent under the experimental conditions.* The catalyzate was collected in an ice-cooled receiver and distilled from a Claisen flask. A crude product was thus obtained in the 150-180° (45 mm) range and completely crystallized at above 0°. Yield up to 70%. Pure p-methyldiphenyl was isolated either by recrystallization from methanol or by fractional distillation in a column.

B.p. 140-141° at 16 mm, m.p. 47.5-48°; λ_{max} 252.25 mμ (ε 21,600) (see Fig. 2). Literature data: b.p. 134-136° (15 mm) [14], 150-153° (17 mm) [15], m.p. 47-48° [16]; λ_{max} 252.3 mμ (ε 21,000) [11].

Found %: C 92.87; H 7.28. $C_{13}H_{12}$. Calculated %: C 92.81; H 7.19.

p-Phenylbenzoic acid, obtained by oxidation of p-methyldiphenyl with 2% potassium permanganate, had m.p. 224-225° (from 60% alcohol).

Found: M 196 (by titration). Calculated: 198.

Aromatization of 2-methyl-5-phenyl-3-hexen-2,5-diol was effected under the same conditions as for the saturated glycol. In view of the considerable decomposition of the glycol, aromatization was conducted in a U-tube (inside diameter 21 mm) immersed in a salt bath. The starting substance was admitted directly to the catalyst zone. Length of catalyst bed 75 mm. The crude product crystallized at below 10° and contained not more than 50% p-methyldiphenyl.

The authors extend their profound thanks to A. S. Nakhmanovich for assistance in the plotting of the absorption spectra and to Yu. M. Faershtein for carrying out the analyses.

*Methanol has been proposed as a solvent for the aromatization of 2,5-dimethyl-2,5-hexanediol in a patent [13], but is less suitable due to the considerable evolution of gas, probably in consequence of its dehydration.

SUMMARY

1. The reaction of aromatization of divinylacetylenic hydrocarbons and of the products of their partial hydrogenation was extended to divinylacetylenes containing an aromatic substituent.

2. Aromatization of 2-methyl-5-phenyl-3-hexyne-2,5-diol, 2-methyl-5-phenyl-3-hexen-2,5-diol and 2-methyl-5-phenylhexane-2,5-diol gave p-methyldiphenyl. For the first time the possibility was thereby demonstrated of catalytic aromatization to hydrocarbons of the diphenyl series of benzenes containing an unsaturated side chain.

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SYNTHESIS OF ORGANOPHOSPHORUS COMPOUNDS FROM HYDROCARBONS AND THEIR DERIVATIVES

XII. OXIDATIVE PHOSPHOCHLORINATION OF HALOGENATED ALKANES

Yu. M. Zinov'ev and L. Z. Soborovskii

We have previously described the oxidative phosphochlorination of some chlorinated paraffinic hydrocarbons [1]. In the present work we studied the reaction of phosphorus trichloride and oxygen with 1,1-di-and 1,1,1-trichloroethanes, 2-chlorobutane, and 1-fluoro-2-chloroethane, as well as with representatives of monofluoro-, bromo- and iodoparaffins. All of these halogenated alkanes, except the iodo derivative, were amenable to oxidative phosphochlorination and gave acid chlorides of the corresponding halogenated alkanephosphinic acids.

$$C_nH_{2n+1}Hal + 2PCl_3 + O_2 \rightarrow C_nH_{2n}HalP(O)Cl_2 + POCl_3 + HCl.$$

Under the reaction conditions the iodoalkanes evidently contain an insignificant quantity of free iodine which inhibits (as previously noted) the oxidation of phosphorus trichloride by oxygen [2]. Therefore butyl iodide (for example) not only does not enter into the reaction in question but also hinders the oxidation of phosphorus trichloride to the oxychloride. Similar results were observed even if the butyl iodide had previously been treated with potassium carbonate and mercury and 5-6 drops of the alkyl halide were introduced per mole of phosphorus trichloride.

Table 1 contains the results of oxidative phosphochlorination of the halogenated alkanes and gives the characteristics of the resulting acid chlorides of haloalkanephosphinic acids. It proved difficult to isolate chlorides (V) and (VI) in the pure state. Their formation by oxidative phosphochlorination of the above-mentioned chlorinated ethanes was confirmed by transformation of (V) and (VI) into the diethyl esters of di- and trichloroethanephosphinic acids respectively.

It was earlier noted that reaction of esters of 2,2-dichloroethanephosphinic acid with triethylamine causes facile cleavage of a mole of hydrogen chloride with formation of derivatives of 2-chloroethenephosphinic acid [4]. Compound (V) likewise contains two chlorine atoms apparently in the 2 position to the phosphorus atom. Treatment with water not only converts (V) into the free acid but also causes dehydrochlorination of the 2,2-dichloroethyl radical. Reaction of (V) with water evidently leads to 2-chloroethenephosphinic acid fluoride [3]. Its structure will be considered in another paper. $Cl_2CHCH_2P(O)Cl_2 + 3H_2O \rightarrow ClCH{=}CHP(O)(OH)_2 + 3HCl.$

In experiments with the product of reaction of 1,1-dichloroethane with phosphorous trichloride and oxygen, the quantity of chlorine found in the aqueous solution was slightly higher than that calculated from the foregoing equation. We may assume that (V) is contaminated with phosphorus oxychloride. This assumption is supported by the low value of carbon and hydrogen in the analysis of the product.

Oxidative phosphochlorination of halo-substituted paraffins, containing several substitutable carbon atoms attached to hydrogen, leads to formation of a mixture of isomeric acid chlorides of the corresponding alkanephosphinic acids. Formation of isomers was more clearly apparent in the oxidative phosphochlorination of 1-bromobutane, the resulting acid chloride boiling over a wide range and the individual fractions not differing in composition. We see from Table 2 that during oxidative phosphochlorination the behavior of 1-bromobutane is entirely like that of 1-chlorobutane and 1-cyanobutane (valeronitrile) whose interaction with phosphorus trichloride and oxygen has already been described [1, 5].

TABLE 1

Compound	Starting haloalkane	Formula	Yield (%)	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	MR_D found	MR_D calc.
(I)	$CH_3CH_2CH_2CH_2Br$	$C_4H_8BrP(O)Cl_2$ *	33.3	109—132° (4)	Individual fractions characterized in Table 2			
(II)	CH_3CHFCH_3	$C_3H_6FP(O)Cl_2$	7.25	80— 83 (19)	1.3091	—	—	34.08
(III)	$ClCH_2CH_2F$	$C_2H_3FClP(O)Cl_2$ **	11.7	98—100 (30)	1.6279	1.4600	33.55	34.33
(IV)	$C_2H_5CHClCH_3$	$C_4H_8ClP(O)Cl_2$ *	35.4	85— 93 (2.5)	1.3903	1.4905	43.57	43.59
(V)	CH_3CHCl_2	$CHCl_2CH_2P(O)Cl_2$	2.0	78— 80 (2)	1.6877	1.4815	37.56	39.22
(VI)	CH_3CCl_3	$CCl_3CH_2P(O)Cl_2$	Low	95 (5)	1.7398	—	—	—

* Mixture of isomeric compounds.

** Compound identical in composition with compound prepared from vinyl fluoride [3]. Its structure will be considered in another paper.

EXPERIMENTAL

1-Bromobutanephosphinic acid chloride (I). Oxygen was passed through a mixture of 68.8 g (0.5 mole) 1-bromobutane and 400 g (2.98 moles) phosphorus trichloride at 0-5° until the reaction ceased. From the reaction mixture was isolated 42.3 g high-boiling oil (I) which came over at 110-145° (4 mm). The fractions characterized in Table 2 were obtained on redistillation.

2-Fluoropropanephosphinic acid chloride (II). 32.0 g (0.51 mole) 2-fluoropropane was condensed into 200 g (1.45 moles) phosphorus trichloride cooled to −20°. Oxygen was passed through the mixture until the reaction ceased. The reaction mixture was cooled at first to −20° and then, after crystals of phosphorus oxychloride had appeared warmed to 0°. 6.7 g of substance was isolated.

Found %: Cl 39.55, 39.75. $C_3H_6OPFCl_2$. Calculated %: Cl 39.68.

1-Fluoro-2-chloroethanephosphinic acid chloride (III). Under the conditions of the first experiment 82.5 g (1 mole) 1-fluoro-2-chloroethane (obtained as in [6]) and 450 g (3.27 moles) phosphorus trichloride gave 9.2 g high-boiling oil (III).

Found %: C 11.60, 11.86; H 2.10, 2.03. $C_2H_3OPFCl_3$. Calculated %: C 12.4; H 1.51.

2-Chlorobutanephosphinic acid chloride (IV). Under the conditions of the first experiment 11.0 g (0.12 mole) 2-chlorobutane (b.p. 68-70°) and 138 g (1 mole) phosphorus trichloride gave 8.0 g of (IV).

Found %: Cl (hydrolyzable) 33.60, 33.61. $C_4H_8OPCl_3$. Calculated %: Cl 33.85.

2,2-Dichloroethanephosphinic acid chloride (V). Under the conditions of the first experiment, 85.8 g (0.88 mole) 1,1-dichloroethane (b.p. 58°) and 433 g (3.15 mole) phosphorus trichloride gave 3.8 g (V). The compound was converted to the diethyl ester of 2,2-dichloroethanephosphinic acid.

Found %: C 8.80, 8.58; H 1.37, 1.32; Cl 54.1, 53.8. $C_2H_3OPCl_4$. Calculated %: C 11.12; H 1.41; Cl (total content) 65.70; anhydridic chlorine 32.85; 3 atoms 49.28%.

Diethyl ester of 2,2-dichloroethanephosphinic acid. 2.7 g (0.0125 mole) of (V) was run at −10° into 25 ml anhydrous alcohol. From the reaction mixture was isolated 0.9 g (31%) of compound.

B.p. 95-97° (4 mm), d^{20}_4 1.2398, $n^{20}D$ 1.4360, MR_D 49.20; calc. 50.51.

Found %: C 30.40, 30.70; H 5.85, 6.26. $C_6H_{13}O_3PCl_2$. Calculated %: C 30.65; H 5.61.

TABLE 2

Boiling range of fractions at 4 mm	Proportion (in % of total yield)	d_4^{20}	n_D^{20}	MR_D	Content* (in %)		
					C	H	Cl
109—113°	13.56	1.6322	1.5103	46.54	19.83	3.60	28.02
113—117	8.52	1.6459	1.5147	46.52	—	—	27.73
120—124	36.05	1.6381	1.5168	46.87	19.35	3.14	29.97
126—129	28.30	1.6443	1.5177	46.71	—	—	28.20
130—132	13.56	1.6607	1.5197	46.45	19.20	3.33	28.11

* Calculated for $C_4H_8OPCl_2Br$ %: C 18.91; H 3.18; Cl 27.93. MR_D 46.48

2,2,2-Trichloroethanephosphinic acid chloride (VI). Under the conditions of the first experiment, 174.6 g 1,1,1-trichloroethane and 358 g phosphorus trichloride gave 1.55 g of (VI). B.p. 95° (5 mm), d^{20}_4 1.7398. The compound was converted to the diethyl ester of 2,2,2-trichloroethanephosphinic acid.

Found %: C 8.32, 8.23; H 1.53, 1.17. $C_2H_2OPCl_5$. Calculated %: C 9.59; H 0.80.

Diethyl ester of 2,2,2-trichloroethanephosphinic acid. 1.0 g (VI) was added to 10 ml cooled anhydrous alcohol. 0.25 g substance was obtained. B.p. 50° (3 mm), $n^{20}D$ 1.4470. The residual oil resinified.

Found %: C 26.67; H 6.08; P 12.58. $C_6H_{12}O_3PCl_3$. Calculated %: C 26.73; H 5.49; P 11.49.

SUMMARY

1. Oxidative phosphochlorination of bromo- and fluoroalkanes and of some mono-, di-, and trichloroalkanes was carried out.

2. The acid chlorides of 1-bromobutane-, 2-fluoropropane-, 1-fluoro-2-chloroethane-, 2-chlorobutane-, 2,2-dichloroethane- and 2,2,2-trichloroethanephosphinic acids were synthesized.

3. It was established that 1-iodobutane not only does not enter into the reaction of oxidative phosphochlorination but also hinders the oxidation of phosphorus trichloride by oxygen.

4. The diethyl esters of 2,2-dichloro- and 2,2,2-trichloroethanephosphinic acids were prepared.

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REACTIONS OF AROMATIC NITRO COMPOUNDS

V. TRANSETHERIFICATION OF ALKYL AND ARYL ETHERS OF 2,4-DINITROPHENOL

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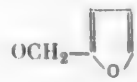
As was established earlier [1], the replacement of one alkoxy group by another in alkyl ethers of 2,4-dinitrophenol goes in such a manner that the alkoxy group with the greater negative inductive effect is displaced. It is naturally of interest to check this rule on other, more complex alkyl and aryl ethers.

The objective of the present investigation was the preparation of suitable alkyl and aryl ethers of 2,4-dinitrophenol by the method of transetherification and the comparison of the electron-donating activities of various alkoxy and aryloxy groups.

The syntheses that were carried out showed that the glycol ether can be prepared only from the phenyl ether; the allyl ether from the phenyl and glycol ethers; and the benzyl ether from the phenyl, glycol, allyl and benzyl ethers. The furfurylether can be obtained from all of the ethers named above, as well as from the primary isoamyl ether of 2,4-dinitrophenol.

Consequently alkoxy and aryloxy groups can be arranged in the following series in respect to substituting activity:



$$> \text{prim. iso } -C_5H_{11}O > \text{n } -C_5H_{11}O > \text{prim. iso } -C_4H_9O >$$
$$> \text{n } -C_3H_7O > C_2H_5O > CH_3O > OCH_2{-}C_6H_5 > OCH_2{-}CH{=}CH_2 >$$
$$> OCH_2{-}CH_2OH > C_6H_5O$$

The behavior of the furfuryl group is especially interesting. The oxygen atom renders the heterocycle as a whole a stronger electron donor than all of the above-mentioned alkoxy and aryloxy groups. It therefore becomes capable of displacing all of the above-mentioned OR groups.

It should be noted that, starting from 2,4-dinitrothioanisole, we were unable to prepare ethers with 2,4-dinitroanisole, glycol or phenol. Unsubstituted 2,4-dinitrothioanisole was obtained in all cases. This interesting fact can be explained by the differing electron affinities of the oxygen and sulfur in the OCH_3 and SCH_3 group respectively. In 2,4-dinitroanisole, due to the electron-accepting activity of the nitro groups, the carbon atom to which the methoxy group is attached becomes positive. In spite of the partial neutralization of the positive charge of the carbon by electrons of the oxygen of the OCH_3 group, the C–O bond still remains polarized, and this facilitates detachment of the methoxy group and its replacement by another OR group. In 2,4-dinitrothioanisole the S–C bond is less polarized due to the lower electron affinity of sulfur, so that the thioanisole group is less easily detached.

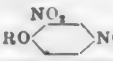
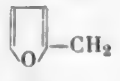
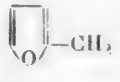
EXPERIMENTAL

General method of preparation of ethers of 2,4-dinitrophenol. 0.01 mole 2,4-dinitrophenyl ether was dissolved in 20 ml benzene and at room temperature there was added dropwise a solution of 0.04 mole potassium

hydroxide in 20-60 ml of the alcohol corresponding to the alkoxy or aryloxy group that it was desired to introduce. After the colored solution had stood for an hour, 50 ml water was added. The benzene layer was washed 3 times with water. The water was separated and the benzene and the excess of the alcohol were distilled off. The residual products were recrystallized from a suitable solvent: glycol ether from benzene, allyl ether from alcohol, benzyl ether from benzene and alcohol, and furfuryl ether from alcohol and glacial acetic acid.

The furfuryl ether of 2,4-dinitrophenol, not previously described was identified by a mixed melting test of the products obtained by transetherification and from 2,4-dinitrochlorobenzene.

In the table are presented data for the ethers of 2,4-dinitrophenol synthesized by the method of transetherification.

Prep. No.	 R in starting ether	R in ether obtained	Yield (in %)	Melting point	
				our data	literature data
1	C_6H_5	$HOCH_2CH_2$	87	110—111°	111—112° [2]
2	$HOCH_2CH_2$	$CH_2{=}CH{-}CH_2$	71	47	46—47 [3]
3	$CH_2{=}CH{-}CH_2$	$C_6H_5CH_2$	65	149—150	149.5 [3]
4	$C_6H_5CH_2$	CH_3	80	94	95 [4]
5	CH_3		83	131—132 (decomp.)	—
6	Prim. iso - C_5H_{11}–		67	131—132 (decomp.)	—

SUMMARY

1. Transetherification is shown to be a simple preparative method of synthesis of diverse ethers of 2,4-dinitrophenol.

2. Replacement of certain alkoxy or aryloxy groups by others depends upon the magnitude of their negative inductive effect.

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[2] British Patent 263191 (1926); Zbl. 1928, I, 2457.

[3] L. C. Raiford and J. C. Colbert, J. Am. Chem. Soc. 48, 2659 (1926).

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REACTIONS OF AROMATIC NITRO COMPOUNDS

VI. THE MECHANISM OF TRANSETHERIFICATION OF ETHERS OF 2,4-DINITROPHENOL

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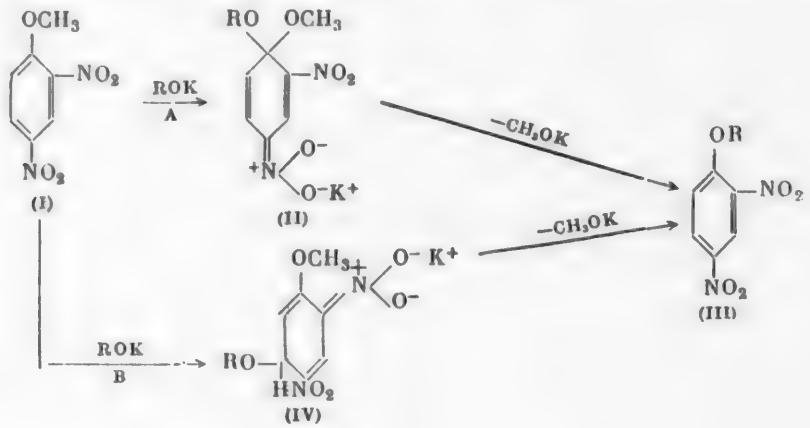
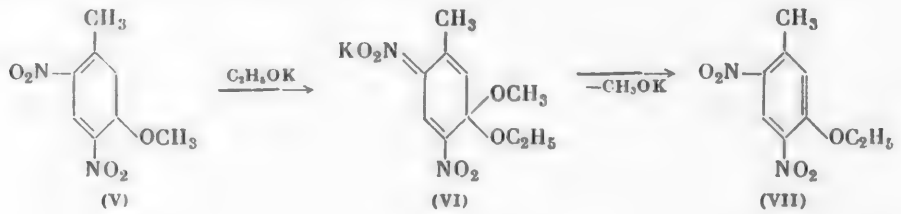
Dnepropetrovsk State University

In preceding papers [1] the theory was advanced that the transetherification of alkyl ethers of 2,4,6-trinitrophenol and 2,4-dinitrophenol goes according to mechanism A. Another transetherification mechanism is that represented by scheme B which excludes formation of addition product (II).

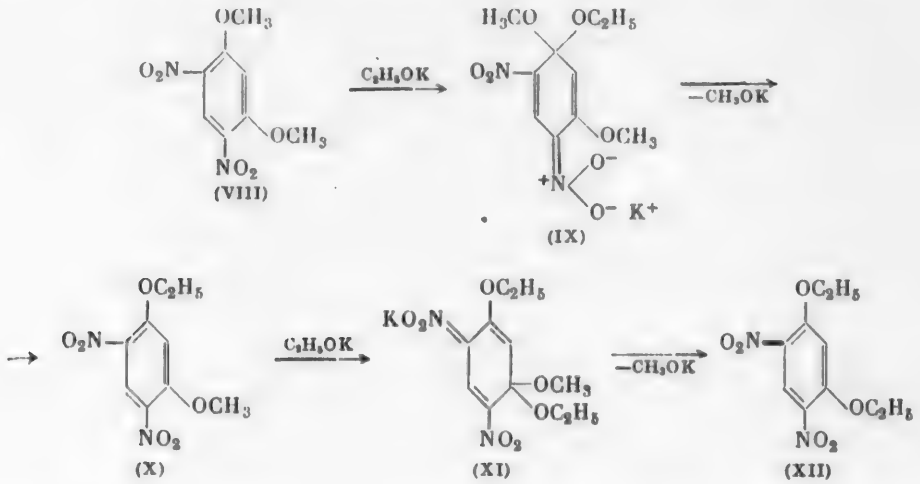


In order to establish which of the two mechanisms is involved in transetherification, it was necessary to select model molecules that would exclude reaction according to one of the proposed schemes. We observed that 2,4-dinitromesitylene does not give colored reaction products with caustic alkali in alcoholic solutions. This indicates that the methyl group hinders the addition of an alkoxy group to the carbon atom of the benzene ring to which it is attached.

If the process goes according to mechanism A, then 3-methoxy-4,6-dinitrotoluene should give 3-ethoxy-4,6-dinitrotoluene as a result of transetherification.

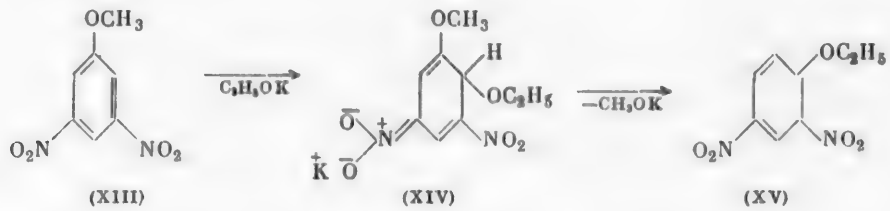


If mechanism B is valid, then the original substance should be recovered since the meta-position to the methoxy group is occupied by a methyl group. Actually, transetherification of (V) gave (VII), so that mechanism A is confirmed. Transetherification of 1,3-dimethoxy-4,6-dinitrobenzene can likewise only proceed by mechanism A.



By transetherification we obtained 1,3-diethoxy-, -dipropoxy-, -dibutoxy- and -diamoxy-4,6-dinitrobenzenes. The ease of transetherification in all of these cases indicates that increase in length of the chain of a normal radical of an alkoxy group does not hinder the reaction, steric hindrance evidently plays only a small part in these cases.

For comparison we studied the action of potassium ethoxide on 3,5-dinitroanisole. Formation of 2,4-dinitrophenetole (XV) would have supported mechanism B.



Recovery of unchanged starting substance (XIII) demonstrates that transetherification does not take place in this case and secondary reactions by mechanism B are excluded. Consequently the only way in which the transetherification reaction can be explained is on the basis of mechanism A.

In order to isolate the products of transetherification of ethers of trinitrophenol, it is necessary to decompose the intermediate product of the reaction with water [1]. Experiments on the transalkylation of 1,3-dimethoxy-4,6-dinitrobenzene in anhydrous ethyl and propyl alcohols and with sodium alcoholate showed that transetherification can also proceed without participation of water.

EXPERIMENTAL

3-Methoxy-4,6-dinitrotoluene (V). a) 34.2 g m-bromotoluene, prepared from p-toluidine [2], was added dropwise to a mixture of 40 g conc. H_2SO_4 (d 1.84) and 26 g fuming HNO_3 (d 1.52) cooled with ice. The mass was stood 18 hours at room temperature. The mixture was then poured onto iced water, and the precipitated 3-bromo-4,6-dinitrotoluene was filtered off and crystallized from alcohol and ligroine. Yield quantitative. M.p. 103-104°.

b) To a solution of 3.3 g 3-bromo-4,6-dinitrotoluene in 200 ml methyl alcohol was added 2.8 g potassium hydroxide in 100 ml methanol. The mass was stirred for half an hour at 40-45°. After cooling, the solution was

poured into water. The precipitated 3-methoxy-4,6-dinitrotoluene was recrystallized from alcohol and ligroine. Yield 80%. M.p. 101-101.5°.

3-Ethoxy-4,6-dinitrotoluene (VII). To a solution of 1.06 g (0.005 mole) 3-methoxy-4,6-dinitrotoluene (V) in 50 ml alcohol was added a solution of 1.12 g (0.02 mole) potassium hydroxide in 30 ml alcohol. After 5 minutes' standing, the mass was poured into 100 ml water. The precipitate was filtered and crystallized from aqueous alcohol and ligroine. Yield 85%. M.p. 95-96° in agreement with the literature [5].

1,3-Dimethoxy-4,6-dinitrobenzene (VIII). a) To a solution of 27.5 g resorcinol in 40-45 ml water at 90° were simultaneously added 129 g methyl ester of benzenesulfonic acid and a solution of 31 g sodium hydroxide in 30 ml water. During this operation it was necessary to keep the medium alkaline. The dimethoxybenzene was distilled with steam and dried over calcium chloride. Yield 91%. B.p. 215°.

b) To 75 ml fuming nitric acid (d 1.52), cooled with a mixture of salt and ice, was added with stirring 12.5 ml dimethoxybenzene dissolved in 12.5 ml carbon tetrachloride at a temperature not higher than 0°. After the addition had been completed (2 hr), the mixture was further stirred 30-40 min at 0°. The resulting dark reaction mass was poured onto ice. Recrystallization from glacial acetic acid gave slightly yellowish, small needles of 1,3-dimethoxy-4,6-dinitrobenzene. Yield 60%. M.p. 155°.

Alkyl ethers of 4,6-dinitroresorcinol. 0.005 mole 1,3-dimethoxy-4,6-dinitrobenzene (VIII) was dissolved in 10-12 ml dioxane with heating. To the solution (cooled to room temperature) was added a cooled solution of 0.02 mole potassium hydroxide in 15 ml of the alcohol corresponding to the alkoxy group introduced into the benzene ring. After 15 minutes' standing, the colored solution was stirred into 50 ml water and stirring was continued for 10 minutes. The reaction products were filtered, washed twice with water and recrystallized from alcohol. The melting points of the unrecrystallized ethyl, n-butyl and n-amyl ethers of 4,6-dinitroresorcinol were close to the literature values [6]; the n-propyl and isobutyl ethers were obtained pure after 2-3 recrystallizations.

The synthesized products and their constants are listed in the table.

Prep. no.	Name of ether of 4,6-dinitroresorcinol	Yield (%)	Melting point	
			our data	literature data
1	1,3-Dimethyl	60	155°	156° [4]
2	1,3-Diethyl	91	130—131	133 [5]
3	1,3-Dipropyl	90	98— 99	100.5 [6]
4	1,3-Dibutyl	93	92— 93	93.5 [6]
5	1,3-Diisobutyl	88	95— 96	96.5 [6]
6	1,3-Diamyl	83	49— 49.5	49 [6]

SUMMARY

1. It was shown that transetherification of ethers of 2,4-dinitro- and 2,4,6-trinitrophenols proceeds through the step of formation of an intermediate product of the quinol type (mechanism A).

2. A new method of preparation of alkyl ethers of 4,6-dinitroresorcinol is proposed.

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STERIC HINDRANCE IN THE 9,9'-BIACRIDINE SERIES

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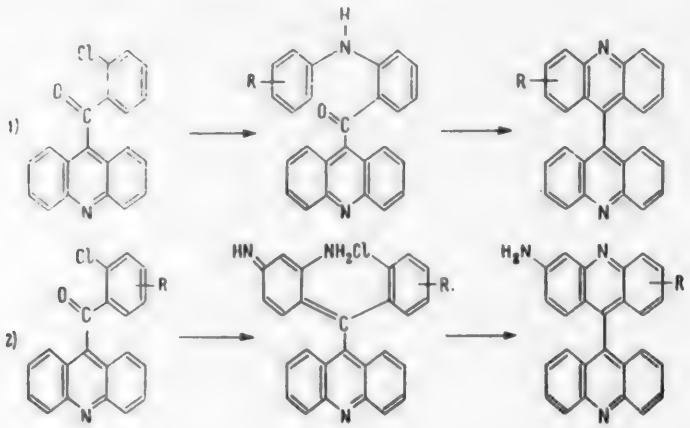
With the objective in mind of expanding the possibilities of study of synthesis in the 9,9'-biacridine series, we attempted to synthesize some unsymmetrical compounds of this series in which the second acridine ring was built in a stepwise fashion. The synthesis schemes chosen by us were based on well studied reactions, which go easily when used to obtain less complex acridine derivatives.



Employing the first scheme given above, we unsuccessfully attampted to condense 9-(o-chlorobenzoyl)-acridine with p-anisidine in the presence of spongy copper. With this catalyst, usually giving good results in the Ullmann reaction, we were unable to condense even 9-(2'-chloro-5'-nitrobenzoyl)acridine with p-anisidine. Negative results were also obtained when cuprous chloride was used as the catalyst. However, in the presence of a mixture of spongy copper and cuprous chloride, the condensation of 9-(2'-chloro-5'-nitrobenzoyl)acridine with aryl amines went very well. It is possible that cupric chloride, present in small amounts in cuprous chloride, is an inhibitor for the reaction, and its reduction by the spongy copper permits restoring the catalytic activity of the cuprous chloride.

In all cases [1] known up to now, a mixture of sulfuric and glacial acetic acids is used to effect the cyclization of 2 anilinoacetophenone and 2-anilinobenzophenone derivatives. We attempted to effect closure of the second acridine ring by treating derivatives of 9-(2'-anilinobenzoyl)acridine with this reagent, but such attempts proved unsuccessful. We were also unable to effect cyclization either by heating with polyphosphoric acid [2], or by long refluxing with phosphorus oxychloride.

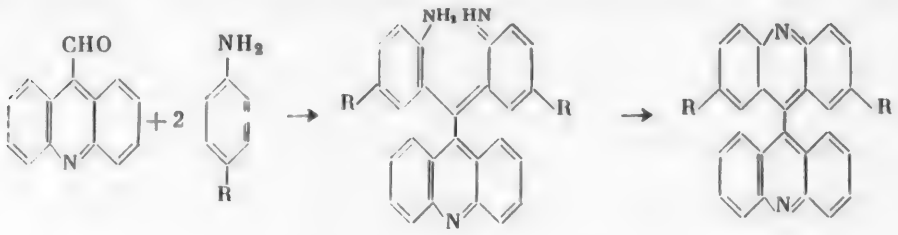
It could be assumed that the difficulties encountered in the cyclization are due either to a decreased reactivity of the CO group, or to a stabilization of the 9-(2'-anilinobenzoyl)acridine derivatives due to the formation of stable hydrogen bonds, $> N-H \cdots N <$, or even of structures of the bipolar ion type. The last assumption

is based on the fact that when these compounds are recrystallized from alcoholic HCl solution, they separate as the free base, and not as the hydrochloride. However, the infrared spectra of crystalline 9-(2'-anilino-5'-nitrobenzoyl)-acridine and 9-(2'-p-toluidino-5'-nitrobenzoyl) acridine show an absorption band at 3318 cm^{-1}, corresponding to only a very slight shift of the characteristic frequency for the NH group. The quite high characteristic frequency of the CO group in these compounds (1712 and 1706 cm^{-1}, respectively) is evidence that the reactivity of the CO group in them should be quite high.

From the above it follows that the difficulty of effecting cyclization of 9-(2'-anilinobenzoyl)acridine derivatives to 9,9'-biacridines, as was mentioned earlier [3] for the case of the carbonyl group in 9-benzoylacridines failing to react with common test reagents, is due to steric factors.

The second scheme given above for the synthesis of unsymmetrical 9,9'-biacridines also failed to give the desired result. We were unable to condense 9-(o-chlorobenzoyl)acridine with m-phenylenediamine. It is quite probable that this reaction also fails to go for steric reasons.

Finally, we attempted to synthesize the desired 9,9'-biacridine derivatives by the scheme:



bearing in mind the fact that A. E. Porai-Koshits and co-workers [4] ran a series of analogous reactions using 9-acridinecarboxaldehyde and arylamines, and when condensation was with m-diethylaminophenol, they obtained the 9-(9'-acridinyl)xanthene derivative. However, we found that the 2,2'-diaminodiphenylmethane derivatives, obtained by us as the result of condensing 9- acridinecarboxaldehyde with p-toluidine and p-anisidine, could not be cyclized. Apparently, in this case also steric hindrance plays an important role, not permitting the amino groups to approach each other. Here it is possible to make comparison with a known fact, where in the case of 2,2'-diaminodiphenyl sulfide derivatives the great distance between the amino groups makes it impossible to effect cyclization with the formation of the phenothiazine ring.

The obtained data permit assuming that steric hindrance renders the synthesis of 9,9'-biacridines via the stepwise construction of the second ring quite improbable.

EXPERIMENTAL

9-(2'-Chloro-5'-nitrobenzoyl)acridine (I). A mixture of 2 g of 9-acridinecarboxylic acid and 20 g of 2-chloro-5-nitrobenzaldehyde was heated under reflux for 20 minutes at 220-230°. The reaction mass was poured into 100 ml of acetone. Then the solution was treated with 5 ml of 42% hydrobromic acid and 1 liter of ether. The obtained precipitate was filtered, washed with ether, dried, and dissolved in 1200 ml of boiling 2% hydrobromic acid. The solution was filtered, and then neutralized with aqueous ammonia. The obtained (I) was filtered, washed with water, and dried in a vacuum-desiccator. We obtained 0.96 g (29.5%) of the compound. After recrystallization from 50% acetone, m.p. 169-170°.

Found %: C 66.62, 66.24; H 3.13, 3.05; N 7.66, 7.44; Cl 9.72. $C_{20}H_{11}O_3N_2Cl$. Calculated %: C 66.21; H 3.06; N 7.72; Cl 9.77.

Hydrobromide: m.p. 295-297° (from 2% hydrobromic acid).

Found %: N 6.01, 6.07; Br 18.46, 18.25. $C_{20}H_{12}O_3N_2ClBr$. Calculated %: N 6.32; Br 18.01.

9-(2'-Anilino-5'-nitrobenzoyl)acridine (II). A mixture of 2 g of (I), 5 ml of aniline, 1 g of spongy copper, 1 g of cuprous chloride and 100 ml of isoamyl alcohol was heated for 6 hours at the boil. After cooling, the precipitate was filtered, washed with a small amount of alcohol, and recrystallized from alcoholic HCl solution. We obtained 1.32 g of (II). The mother liquors gave an additional 0.25 g of (II). After treatment with alcoholic ammonia, followed by recrystallization from alcohol, the m.p. was 290-292°. Total yield 1.57 g (68.0%).

Found %: C 74.79, 74.62; H 4.00, 4.19; N 9.67, 10.01. $C_{26}H_{17}O_3N_3$. Calculated %: C 75.45; H 4.08; N 10.02.

9-(2'-p-Toluidino-5'-nitrobenzoyl)acridine (III). Using the same conditions as for the synthesis of (II), we obtained 0.55 g (65.7%) of (III) from 0.7 g of (I) and p-toluidine. After recrystallization from alcohol, m.p. 341-342°.

Found %: C 74.49; H 4.48; N 9.82. $C_{27}H_{19}O_3N_3$. Calculated %: C 74.81; H 4.42; N 9.70.

9-(2'-p-Anisidino-5'-nitrobenzoyl)acridine (IV). Using the same conditions as for the synthesis of (II), we obtained 0.25 g (28.8%) of (IV) from 0.7 g of (I) and p-anisidine. After recrystallization from alcohol, m.p. 321-323°.

Found %: N 10.00. $C_{27}H_{19}O_4N_3$. Calculated %: N 9.35.

9-Acridinyl(2'-amino-5'-methylphenyl) (2"-imino-5"-methylphenylene)methane (V). A mixture of 1 g of acridinecarboxaldehyde, 5 g of p-toluidine and 1 g of fused ground zinc chloride was heated, with stirring, for 2 hours at 140-150°. The reaction mixture was then treated with 50 ml of water, the mixture heated to the boil, and cooled. The precipitate was filtered, and then treated twice with 50 ml of boiling alcohol. The insoluble portion was digested with boiling 2 N hydrochloric acid, the hot solution filtered, and the filtrate neutralized with ammonia. The resulting precipitate was filtered, washed with water, then with a little alcohol, and dried. We obtained 0.2 g (13.4%) of (V). M.p. 304-305°. The alcohol mother liquor was worked up in customary manner to give 0.26 g (22.1%) of (VI) hydrochloride, m.p. 237-240°.

Found %: C 83.34, 83.21; H 5.49, 5.48; N 11.02. $C_{28}H_{23}N_3$. Calculated %: C 83.75; H 5.77; N 10.46.

9-Acridinyl(2'-amino-5'-methoxyphenyl) (2"-imino-5"-methoxyphenylene)methane (VII). Using the same conditions as for the synthesis of (V), we obtained 0.27 g (24.5%) of (VII), m.p. 183-185°, from 1 g of (VI) and p-anisidine. We also recovered 52.8% of unchanged (VI).

Found %: C 77.23, 77.34; H 4.98, 5.18; N 9.43. $C_{28}H_{23}O_2N_3$. Calculated %: C 77.57; H 5.34; N 9.69.

SUMMARY

1. Steric hindrance is an important factor in constructing the second acridine ring in 9,9'-biacridines. It is responsible for the failure to synthesize unsymmetrical 9,9'-biacridines by the stepwise construction of the second ring.

2. It was shown that a mixture of spongy copper and cuprous chloride is a more active catalyst in the Ullmann reaction than are the other catalysts, usually used in this reaction.

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COMPLEXES OF SULFONAMIDES WITH AMINES

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Sisler and Rosenbaum [1], in studying the fusibility of the system $SO_2(NH_2)_2-NH_3$, revealed that the compounds $SO_2(NH_2)_2 \cdot 2NH_3$ and $SO_2(NH_2)_2 \cdot 3NH_3$ exist in it. A. V. Kirsanov and Yu. M. Zolotov [2] mention that although they were unable to isolate the addition products of sulfamide to pyridine, still a definite reaction takes place between the indicated compounds, and they postulated a structure for the hypothetical addition product involving hexavalent sulfur with a coordination number of 5 [3].

We postulated that organic sulfonamides should also form complexes with amines, and set ourselves the task of attempting to isolate some of these complexes and study their properties. We were able to obtain such complexes for the case of sulfanilamide with pyridine, di-(p-carbomethoxyaminobenzenesulfonyl)iminothiazoline with pyridine, and di-(p-acetamidobenzenesulfonyl)iminothiazoline with diethylamine. In the last two cases, the nitrogen of the sulfonamido groups fails to contain a hydrogen atom. The ability of such sulfonamide derivatives to form complexes with amines is definite proof that the linkage between nitrogen and the amine is created without involving a proton.

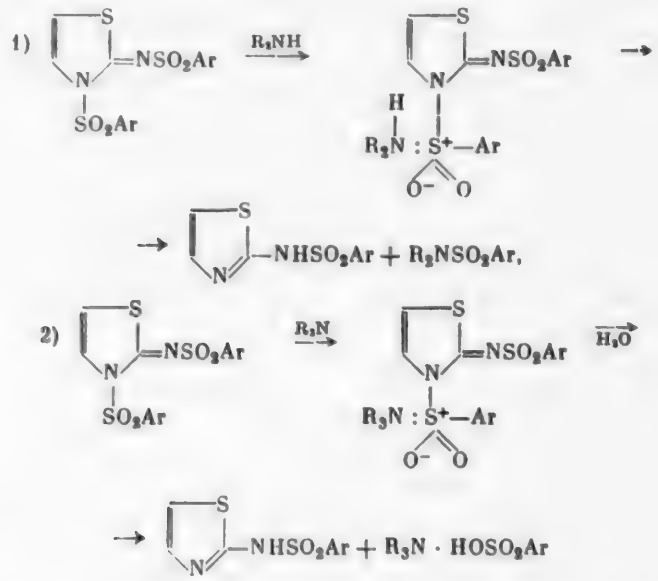
Kirsanov and Zolotov [4] have shown that the amidation of carboxylic acids with sulfamide is greatly facilitated in the presence of pyridine; but at the same time they confirmed the conclusion made by Oxley and others [5, 6] that it is possible to effect the amidation of carboxylic acids with arylsulfonamides only under very drastic conditions. In the studies of Kirsanov and co-workers it was shown that, in the presence of pyridine, the amidation of carboxylic acids with sulfamide derivatives also goes in the case of sym-diphenylsulfamide [7]; in the case of unsym-dimethylsulfamide only the dimethylamides of carboxylic acids are formed [8], even though the reaction does not go with tetrasubstituted sulfamides [9].

On the basis of this information, we postulated that the formation of complexes with amines should substantially weaken the S–N bond in the sulfonamido group and, as a result, facilitate certain reactions that go with difficulty for a number of organic sulfonamides. Realizing the stability of the S–N bond in arylsulfonamides, we deemed it would be easiest to show its weakening by employing diarylsulfonamidoiminothiazoline derivatives. As is known, one of the arylsulfonyl groups in these compounds is cleaved with comparative ease when exposed to the action of various reagents. Actually, when the complex of di-(p-acetamidobenzenesulfonyl)iminothiazoline with diethylamine is heated in aqueous medium, the complex suffers cleavage very rapidly, leading to the formation, in high yield, of both 2-(p-acetamidobenzenesulfonamido)thiazole and the diethylamide of N-acetylsulfanilic acid.

Easy dissociation probably also prevails when the complex of di-(p-carbomethoxyaminobenzenesulfonyl)-iminothiazoline with pyridine is heated in aqueous medium. For this reason we were unable to follow the transformation of the pure complex. However, in the presence of excess pyridine, di-(p-carbomethoxyaminobenzenesulfonyl)iminothiazoline suffers rapid hydrolysis with the formation of 2-(p-carbomethoxyaminobenzenesulfonamido)-thiazole. Since di-(p-carbomethoxyaminobenzenesulfonyl)iminothiazole, in contrast to di-(p-acetamidobenzenesulfonyl)iminothiazoline, is quite stable toward alkaline reagents, it is obvious that the ease of hydrolysis in the presence of pyridine is due to the intermediate formation of a complex.

The S–N bond in di-(p-acetamidobenzenesulfonyl)iminothiazoline is easily cleaved in the presence of excess aniline in aqueous medium; here both 2-(p-acetamidobenzenesulfonamido)thiazole and the anilide of N-acetylsulfanilic acid were isolated in high yield. At the same time, reaction with excess α-aminopyridine in aqueous medium led only to hydrolysis, analogous to the hydrolysis with aqueous pyridine.

Evidently, all of these transformations go with the intermediate formation of complexes between the sulfonamides and the amines, and a hypothetical mechanism for these transformations can be depicted by the following schemes:



Reactions with primary and secondary amines should go according to the first scheme, while reactions with tertiary amines should go according to the second scheme. The fact that the reaction with α-aminopyridine goes according to the second scheme can be explained by the more probable formation of a linkage involving the ring nitrogen, rather than the nitrogen of the amino group.

It is known [10] that the reaction of 2-aminothiazole with arylsulfonyl chlorides in aqueous medium leads to the formation of diarylsulfonyliminothiazolines, and when reaction is in pyridine – to 2-arylsulfonamidothiazoles. From the viewpoint of the mechanism proposed by us, this fact can be explained by stating that, in pyridine medium, only the first formed complex of diarylsulfonyliminothiazoline with pyridine is capable of easily reacting with a second molecule of 2-aminothiazole to yield the 2-arylsulfonamidothiazole.

EXPERIMENTAL

Complex of sulfanilamide with pyridine. Two grams of sulfanilamide was dissolved in 10 ml of dry pyridine in the cold. The solution was diluted with 50 ml of hexane. A greenish-yellow oil separated, which gradually crystallized when cooled in ice (colorless crystals). The precipitate was filtered, washed with hexane, and dried in a vacuum desiccator. The yield was 2.87 g (97.8%), m.p. 128-130° (softens at 38-40°). A pyridine odor develops when the compound is kept in the air.

Found pyridine 33.0%.* $C_6H_8O_2N_2S \cdot C_5H_5N$. Calculated pyridine 31.45%

Complexes of di-(p-acetamidobenzenesulfonyl)iminothiazoline (I):

With diethylamine. a) Two grams of recrystallized (from methanol) di-(p-acetamidobenzenesulfonyl)-iminothiazoline (m.p. 138-140°) was mixed with 10 ml of diethylamine. Evolution of heat was observed. An oil separated from the solution, which gradually crystallized. The precipitate was filtered, washed with ether, and dried in a vacuum desiccator. Yield 1.1 g, m.p. 133-135°.

*The amount of amines in the complexes was determined acidimetrically.

Found diethylamine 18.7%. $C_{19}H_{18}O_6N_4S_3 \cdot 2(C_2H_5)_2NH$. Calculated diethylamine 22.8%.

Cleavage. A mixture of 2.4 g of the complex and 20 ml of water was heated for 5 minutes on the boiling water bath. The insoluble portion, an oil that gradually crystallized when cooled, was filtered, washed with water, and air-dried. We obtained 1.0 g (87.8%) of the diethylamide of N-acetylsulfanilic acid, m.p. 79-81°. Acidification of the filtrate with hydrochloric acid gave 1.02 g (80.2%) of 2-(p-acetamidobenzenesulfonamido)thiazole, m.p. 252-253°.

b) A mixture of 7.5 g of (I), 3.5 g of diethylamine and 50 ml of water was heated, with stirring, for 5 minutes at 70°. Here a substantial portion of the precipitate dissolved. The insoluble portion, an oily liquid that gradually crystallized when cooled, was filtered, washed with water, and air-dried; the substance was identified as being the diethylamide of N-acetylsulfanilic acid. Yield 3.74 g (91.5%). After recrystallization from 40% alcohol, m.p. 81-82° [10]. Acidification of the filtrate with hydrochloric acid gave 4.0 g (89%) of 2-(p-acetamidobenzenesulfonamido)-thiazole. M.p. 249-251° [11].

With aniline. A mixture of 7.5 g of (I), 3.5 g of aniline and 50 ml of water was heated, with stirring, for 5 minutes at 100°, after which the mixture was diluted with 250 ml of water, and cooled. The precipitate was filtered, and then treated with ammonia solution. The insoluble portion was filtered, washed with water, and dried. We obtained 3.6 g (81.8%) of the anilide of N-acetylsulfanilic acid. After recrystallization from alcohol, m.p. 211-212° [12]. Acidification of the ammoniacal solution with hydrochloric acid gave 3.97 g (88%) of 2-(p-acetamidobenzenesulfonamido)thiazole, m.p. 249-251°.

With α-aminopyridine. A mixture of 7.5 g of (I), 3.5 g of α-aminopyridine and 50 ml of water was heated, with stirring, for 1 hour on the boiling water bath. After cooling, the mixture was treated with ammonia solution to dissolve the 2-(p-acetamidobenzenesulfonamido)thiazole,* while the insoluble portion was filtered, washed with water, and dried. We recovered 4.4 g of unreacted (I), m.p. 130-131°. Acidification of the ammoniacal solution with hydrochloric acid gave 1.5 g (80.6%) of 2-(p-acetamidobenzenesulfonamido)thiazole, m.p. 249-251°.

Complexes of di-(p-carbomethoxyaminobenzenesulfonyl)iminothiazoline:

With pyridine. a) Two grams of di-(p-carbomethoxyaminobenzenesulfonyl)iminothiazoline was dissolved in 10 ml of dry pyridine in the cold. The solution was diluted with 50 ml of hexane, and the obtained precipitate was filtered, washed with hexane, and dried in a vacuum desiccator. Yield 2.20 g (94%), m.p. 218-220°. A pyridine odor develops when the complex is kept in the air.

Found pyridine 14.75%. $C_{19}H_{18}O_8N_4S_3 \cdot C_6H_5N$. Calculated pyridine 13.78%.

b) A mixture of 4 g of di-(p-carbomethoxyaminobenzenesulfonyl)-iminothiazoline, 10 ml of water and 10 ml of pyridine was heated for 30 minutes on the boiling water bath. After cooling, the mixture was treated with 2% NaOH solution to dissolve the 2-(p-carbomethoxyaminobenzenesulfonamido)thiazole.** The precipitate dissolved completely. Acidification of the solution gave 2.3 g (96%) of 2-(p-carbomethoxyaminobenzenesulfonamido)thiazole, m.p. 250-251° [13].

SUMMARY

1. Apparently, all sulfonamides possess the ability to form complexes with amines.

2. In the complexes of sulfonamides with amines, the S—N bond of the sulfonamido group is weakened and is more susceptible to attack by different reagents. The heating of the complexes of sulfonamides with primary and secondary amines can lead to rupture of the S—N bond in the sulfonamido group and the formation of a new sulfonamide; the complexes of sulfonamides with tertiary amines are hydrolyzed with comparative ease to yield salts of the corresponding sulfonic acids.

*(I) fails to react with aqueous ammonia solution in the cold to yield 2-(p-acetamidobenzenesulfonamido)-thiazole and N-acetylsulfanilamide.

**Di-(p-carbomethoxyaminobenzenesulfonyl)iminothiazoline is not hydrolyzed by dilute NaOH solution in the cold.

3. Schemes for the mechanism of the transformations suffered by complexes of sulfonamides with amines were proposed.

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STUDY OF THE CHEMICAL STRUCTURE OF VARIOUS FRACTIONS OF SODIUM BUTADIENE RUBBER

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A comparative study of the degree of branching shown by butadiene rubber macromolecules is of both great scientific and practical interest, since this problem is associated with understanding the mechanism of polymerization and the relationships that exist between the structure and the properties of high-molecular compounds. Using physical and physicochemical methods, branching has been studied by many investigators [1].

I. Ya. Poddubnyi and co-workers came to the conclusion that highly branched or structured molecules are present in the higher fractions of sodium butadiene rubber [2].

In this paper we made a comparative study of the chemical structure of eight fractions of sodium butadiene rubber for the purpose of determining their degree of branching.

The method of fractional precipitation [3] was used to separate the different fractions of sodium butadiene rubber (Table 1).

We used the ozonolysis method to study the chemical structure of the isolated fractions, subjecting the obtained ozonides to oxidative decomposition [4, 5], and the acids (levulinic, acetic, formic, succinic, 1,2,4-butanetricarboxylic, 1,2,3-propanetricarboxylic, 1,2,4,6-hexanetetracarboxylic) isolated from such decomposition were then separated by the method of partition chromatography [6, 7], after which the percent of polymer carbon skeleton contained in them was calculated from the chromatograms (Table 2).

Succinic, 1,2,4-butanetricarboxylic, and 1,2,4,6-hexanetetracarboxylic acids were formed from the 1,4–1,4; 1,4–1,2–1,4, and 1,4(1,2)$_2$–1,4 fragments, respectively. Levulinic acid appears as the abnormal ozonolysis product of the 1,4–1,2–1,4 fragment [8]. 1,2,3-Propanetricarboxylic acid can be the abnormal ozonolysis product of the 1,4–1,2–1,4 fragment [9], or it can be formed from the 1,4–1,4 fragment branched at the α-methylene group [8] as the result of metalation during the polymerization process (in the presence of metallic sodium), in accordance with the following scheme.

$$-CH_2-CH=CH-CH_2-CH_2-CH=CH-CH_2- \xrightarrow{Na \text{ or } NaR}$$

$$\rightarrow -CH_2-CH=CH-\underset{\displaystyle Na}{\underset{|}{CH}}-CH_2-CH=CH-CH_2- \xrightarrow{C_4H_6}$$

$$\rightarrow -CH_2-CH=CH-\underset{\displaystyle CH_2-CH=CH-CH_2Na}{\underset{|}{CH}}-CH_2-CH=CH-CH_2-$$

For all of the isolated fractions, it was found that the obtained 1,2,3-propanetricarboxylic acid contains about 7.5% of the polymer carbon skeleton, of which apparently about 4.5% is the ozonolysis product of the 1,4–1,4 fragments, branched at the α-methylene group, while the remainder (3.0%) are the abnormal ozonolysis products of the 1,4–1,2–1,4 fragment [10].

For all of the isolated fractions, the chromatograms of the mixture of acids, obtained in the oxidative decomposition of the ozonides, proved to be practically identical, both as regards the number of peaks, and as regards the relative height of the latter, and for this reason we give here only the chromatogram of the 1st fraction. All of the chromatograms of the mixed acids have ten peaks (Table 2), of which seven peaks (II, III, IV, V, VI, VII, VIII) correspond to identified acids, while the other three peaks (I, IX, X) correspond to acids whose structure was not determined. Both the total unsaturation and percent of external double bonds are practically the same in all of the fractions (Table 1). Since the percent of polymer carbon skeleton, found on the basis of 1,2,3-propanetricarboxylic acid, ranges within the limits 7.2-7.9%, i.e., is practically constant, and since studying the chemical structure in the different fractions was run under strictly comparable conditions, it can be assumed that the degree of branching at the α-methylene group is the same in the different fractions.

EXPERIMENTAL

The sodium butadiene rubber taken for study had been obtained at 40°, and had a Karrer plasticity of 0.12. The rubber was purified by dissolving twice in benzene, and then precipitating with alcohol, after which it was dried to constant weight in vacuo (1 mm) at room temperature. The average molecular weight of the purified rubber was determined by the viscosity method [3]. In addition, we determined the elementary composition, the total unsaturation by the Kemp–Vasil'ev method [11], and the percent of external double bonds* by infrared spectroscopy [12] and by ozonolysis [13] (Table 1).

TABLE 1

Fraction No.	Molecular weight	Elementary composition (%)		Total unsaturation	Percent external double bonds	
		C	H		infrared spectroscopic data	ozonolysis data
1-st	835000	88.01	11.34	89.8	67.9	66.8
2-nd	665000	87.83	11.23	89.6	70.2	—
3-rd	480000	87.71	11.15	87.0	70.4	—
4-th	391000	87.97	11.22	85.6	71.6	—
5-th	304000	87.36	11.42	84.3	72.3	—
6-th	195000	87.30	11.29	83.8	69.2	—
7-th	105000	86.99	11.40	82.3	72.0	70.0
8-th	about 20000	86.90	11.41	84.2	70.0	—
Unfractionated rubber	400000	88.00	11.29	86.6	70.0	69.0

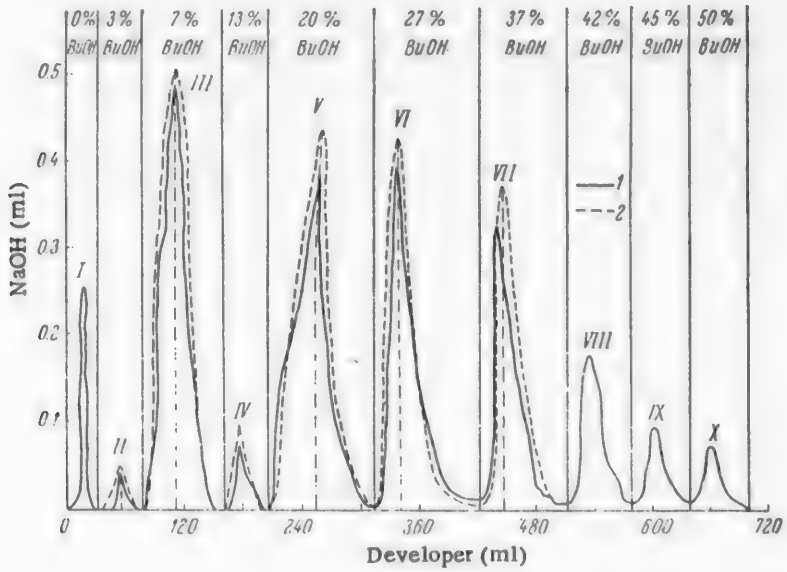
Fractional precipitation of the rubber was run in an oxygen-free nitrogen atmosphere [3, 14]. We obtained eight fractions with gradually decreasing molecular weight. Each fraction was characterized.

The chemical structure of the unfractionated rubber and of the different isolated fractions was determined by the ozonolysis method [4, 5]. The ozonization was run in ethyl acetate, in which the obtained ozonides are soluble, and after distilling off the solvent in vacuo they were obtained as colorless, clear, viscous substances. The ozonides were decomposed with acetyl hydroperoxide (60%) in the presence of glacial acetic acid [4, 15]. The products of the oxidative decomposition of the ozonides were studied by the method of partition chromatography [16, 17], using a column (h = 400 mm and d = 17 mm) filled with silica gel (180 mm long), labeled "course-pored fine silica gel" (Voskresenskii Chemical Combine), that had been sifted through a 200-300 mesh screen. The mixture of acids, obtained from the oxidative decomposition of the ozonides of both the

* $\overline{-CH_2-CH=CH-CH_2-}$ represents the link with internal double bond, while $-CH_2-\underset{\displaystyle H_2C=CH}{\overset{\displaystyle |}{CH}}-$ is the link with external double bond.

unfractionated rubber and the isolated fractions, was dissolved in tertiary amyl alcohol. One milliliter of the solution was placed in the chromatographic column, and then chloroform, containing a constantly increasing amount of n-butyl alcohol, was passed through the column at a rate of 1 ml per minute. The effluent solution from the column was titrated in 3 ml portions with an alcoholic solution of 0.017 N NaOH in the presence of phenolphthalein. The recovery of acids after their elution from the column with mobile solvent was 98-99% [6, 7].

We have plotted the results obtained by chromatographing: along the ordinate we have plotted the ml of NaOH solution consumed for titration of the taken sample, while along the abscissa we have plotted the ml of mobile solvent. The chromatogram of our hypothetical mixture ("artificial" mixture) of levulinic, acetic, formic, succinic, 1,2,4-butanetricarboxylic and 1,2,3-propanetricarboxylic acids (Fig.) was obtained under the same conditions as the chromatogram of the investigated acids.



Chromatogram of mixture of acid products from the ozonolysis of the 1st fraction of sodium butadiene rubber and chromatogram of artificial mixture of acids. 1) Chromatogram of mixture of acid ozonolysis products, 2) chromatogram of artificial mixture of acids. Designation of peaks: II) levulinic, III) acetic, IV) formic, V) succinic, VI) 1,2,4-butanetricarboxylic, and VIII) 1,2,4,6-hexanetetracarboxylic acids. Peaks I, IX and X were not identified.

The acids, found in the investigated mixtures, were identified chromatographically, by the technique of comparing the chromatograms of the investigated mixture with the chromatograms of the "artificial" mixture on the basis of the peaks of the volume and threshold elutions of each acid [6, 17]. The validity of such chromatographic identification had been confirmed earlier by chemical analysis data [8, 18]. The chromatographic results are shown in the figure.

From the chromatogram, plotted on the basis of the titration data, we calculated the amount of each acid and its carbon content. From a comparison of the amount of carbon in the acid with that contained in the ozonized rubber, we calculated the percent of carbon skeleton in the acid and the percent of carbon skeleton of polymer in the separate portions of the macromolecule (Tables 2 and 3).

The identification of levulinic acid chromatographically was confirmed by chemical analysis. As the result of many experiments, sufficient levulinic acid to permit preparation of the sodium salt was obtained, which was then converted to the silver salt.

Calculated %: C26.91; H 3.14; O21.52; Ag 48.43. $C_5H_7O_3Ag$. Found %: C 26.82, 26.94; H 3.34, 3.24; O 21.64, 21.54; Ag 48.20, 48.28.

Both the unfractionated rubber and the isolated fractions were shown to contain 1,4−1,4; 1,4−1,2−1,4, and 1,4−$(1,2)_2$−1,4 fragments, branched at the α-methylene group.

TABLE 2

Peak No.	Name of acid / Fraction No.	Percent of polymer carbon skeleton in the acids, obtained in the ozonolysis of the isolated fractions and of unfractionated rubber								
		1	2	3	4	5	6	7	8	unfractionated rubber
II	Levulinic	0.4	0.8	0.5	0.4	0.4	1.02	0.7	1.6	0.7
III	Acetic	Not determined, since the oxidative decomposition of the ozonides was run in acetic acid								
IV	Formic									
V	Succinic	11.6	11.9	10.6	11.2	10.6	11.4	12.4	12.7	11.8
VI	1,2,4-Butanetricarboxylic	11.0	12.4	11.3	12.0	11.5	11.5	11.3	11.3	11.9
VII	1,2,3-Propanetricarboxylic	7.6	7.4	7.4	7.6	7.5	7.8	7.2	7.9	7.4
VIII	1,2,4,6-Hexanetetracarboxylic	2.3	2.5	2.6	4.7	3.3	3.4	3.7	4.1	4.0

TABLE 3

Structure of fragments / Fraction	Percent of carbon skeleton in fragments								
	1	2	3	4	5	6	7	8	unfractionated rubber
1,4—1,4	11.6	11.9	10.6	11.2	10.6	11.4	12.4	12.7	11.8
1,4—1,2—1,4	12.6	14.2	13.0	13.7	13.2	13.2	13.0	13.0	13.6
1,4—$(1,2)_2$—1,4	2.8	3.0	3.1	5.6	4.0	4.1	4.4	4.9	4.8

SUMMARY

1. Sodium butadiene rubber, obtained at 40°, was separated by fractional precipitation into eight fractions, with a molecular weight ranging from 835,000 to 20,000. Infrared spectroscopy and ozonolysis were used to determine the percent of (1,2) links, and this value was found to be practically the same for all of the fractions.

2. It was established by ozonolysis that all of the investigated fractions contain macromolecular fragments with the same structure and same relative size.

3. It was found that all of the fractions contain macromolecular fragments that show branching of the α-methylene groups and, in addition, have practically the same relative size, from which it follows that the branching of the investigated fractions is the same.

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SYNTHESIS OF SOME ACYL DERIVATIVES OF PHENOTHIAZINE

I. DERIVATIVES OF GLYCINE AND α-ALANINE, CONTAINING QUATERNARY NITROGEN ATOMS

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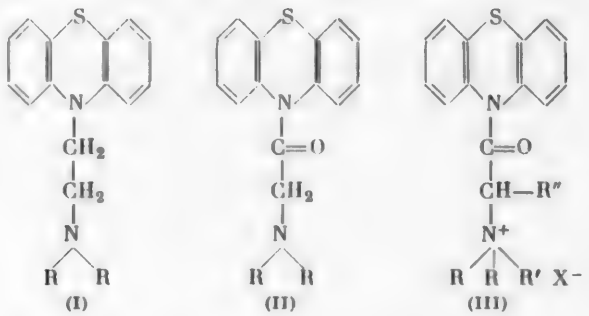
Considerable attention has been given recently to phenothiazine derivatives, containing different substituents on the nitrogen of the thiazine ring [1, 2]. Phenothiazine derivatives of type (I) and (II) are of special interest here, possessing strong cholinolytic action [1].



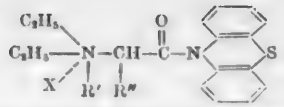
(I) (II) (III)

In this paper we describe the preparation and properties of some new compounds of type (III), being salts of quaternary ammonium bases: when R" = H, these compounds are substituted glycine derivatives, and when R" = CH_3, they are substituted α-alanine (d, l) derivatives. As alkyl radicals, linked to the quaternary nitrogen, we introduced methyl and ethyl: R' = CH_3 or C_2H_5, and R = C_2H_5.

The indicated compounds were synthesized by the following scheme: the reaction of phenothiazine with either chloroacetyl chloride or α-bromopropionyl bromide gave the corresponding α-haloacyl derivative of phenothiazine, and then the halogen was replaced by the diethylamino group by reaction with excess diethylamine. The obtained diethylaminoacetyl- or α-diethylaminopropionyl-10-phenothiazine was then reacted with methyl iodide, dimethyl sulfate, or ethyl iodide. The compounds obtained in this manner represented either the iodides (III, X = I), or the methosulfates (III, X = CH_3SO_4), of the quaternary ammonium derivatives.

The characteristic properties of the obtained quaternary compounds (III), and also of the salts of the corresponding tertiary amines, are given in the table. The iodides of the quaternary derivatives (table, compounds 2, 3, 8 and 9) are much less soluble in water than the methosulfates. Due to their good solubility in water, the methosulfates could be converted to more difficulty soluble salts by treatment of their aqueous solutions with other anions. Thus, the addition of concentrated aqueous solutions of potassium iodide, sodium bromide, or sodium nitrate to a water solution of diethylaminoacetyl-10-phenothiazine dimethosulfate (table, compound 4) gave the corresponding salts (iodide, bromide, or nitrate) of this quaternary base (table, compounds 2, 5 and 6).

All of the synthesized quaternary ammonium derivatives, as well as the corresponding salts of the tertiary amines (table, compound 7), were tested pharmacologically by M. Ya. Mikhel'son. They all function as powerful



Compound No.	X-	R′	R″	Formula	Melting point	Solubility at 20°	Color
1	Cl	H	H	$C_{18}H_{21}ON_2SCl$	185—186°	Readily in water and alcohol	White
2	I	CH_3	H	$C_{19}H_{23}ON_2SI$	187—189	0.25—0.3% in water, readily in alcohol	Light yellow
3	I	C_2H_5	H	$C_{20}H_{25}ON_2SI$	180—182	0.3% in water, readily in alcohol	White
4	CH_3 | SO_4	CH_3	H	$C_{20}H_{26}O_5N_2S_2$	101—102	Readily in water and alcohol	White
5	Br	CH_3	H	$C_{19}H_{23}ON_2SBr$	105—107	0.3—0.4% in water, readily in alcohol	White
6	NO_3	CH_3	H	$C_{19}H_{23}O_4N_3S$	183—184	0.5% in water, readily in alcohol	White
7	Cl	H	CH_3	$C_{19}H_{23}ON_2SCl$	190—191	Readily in water and alcohol	White
8	I	CH_3	CH_3	$C_{20}H_{25}ON_2SI$	90—95 decomp.	0.25% in water, 3—4% in alcohol	Yellow
9	I	C_2H_5	CH_3	$C_{21}H_{27}ON_2SI$	197—199	0.25—0.3% in water, readily in alcohol	White with a yellow cast

cholinolytic agents, in which connection the quaternary derivatives show a predominantly peripheral action, while the tertiary derivatives also penetrate into the brain, and for this reason show a central cholinolytic action [3].

EXPERIMENTAL

10-(Chloroacetyl)phenothiazine (see [1]). A solution of 46 g of phenothiazine in 450 ml of benzene was heated under reflux for 3 hours with 37 g (25 ml) of chloroacetyl chloride. After removal of the solvent, the obtained product was recrystallized from alcohol, m.p. 116-117°. Yield 60 g (95%).

10-(Diethylaminoacetyl)phenothiazone. A mixture of 38 g of chloroacetylphenothiazine and 36.5 g (50 ml) of diethylamine in 350 ml of alcohol was heated under reflux for 1.5 hours. Then 4.5 g of calcined sodium carbonate was added to the mixture (to decompose the formed diethylamine hydrochloride), and the mixture heated for another 1.5 hours.*

After removal of the solvent, the obtained base was purified by dissolving in dilute hydrochloric acid, followed by precipitation with 10% sodium carbonate solution. M.p. 56-57° (from alcohol).

10-(Diethylaminoacetyl)phenothiazine hydrochloride was obtained in 85-90% yield by dissolving the free diethylaminoacetylphenothiazine base in 5% alcoholic hydrochloric acid solution. After removal of solvent (at room temperature), the salt was filtered, and washed with anhydrous alcohol and ether. White crystals (m.p. 185-186°), readily soluble in water and alcohol. Its solutions show neutral.

Found %: Cl 10.8, 10.09. $C_{18}H_{21}ON_2SCl$. Calculated %: Cl 10.18.

On the basis of the positive pharmacological test data, it was decided by the Pharmacology Committee to test the obtained compound (under the name of "diphazine") clinically.

10-(Diethylaminoacetyl)phenothiazine methiodide. The product was obtained in 60% yield by heating the free diethylaminoacetylphenothiazine in alcohol with excess methyl iodide for 2 hours. The compound was purified by treatment with ether, followed by recrystallization from a mixture (1 : 1) of alcohol and water. The

*The author of [1] ran the reaction in benzene, filtered from the diethylamine hydrochloride, and extracted the base with hydrochloric acid.

compound was obtained as a pale yellow crystalline powder (m.p. 187-189°), difficultly soluble in water at room temperature, and readily soluble in alcohol.

Found %: I 28.76, 28.00. $C_{19}H_{29}ON_2SI$. Calculated %: I 28.00.

10-(Diethylaminoacetyl)phenothiazine ethiodide was obtained by heating the free diethylaminoacetylphenothiazine in alcohol with excess ethyl iodide for 3 hours. The mass remaining after removal of the solvent was treated with ether and alcohol, and then recrystallized from a mixture (1 : 1) of alcohol and water. M.p. 180-182°. White crystalline powder, difficultly soluble in water (0.3% at 20°), and readily soluble in hot alcohol. Yield 45-50%.

Found %: I 27.00, 27.43. $C_{20}H_{25}ON_2SI$. Calculated %: I 27.13.

10-(Diethylaminoacetyl)phenothiazine dimethosulfate. With ice water cooling, a solution of 2.7 g of dimethyl sulfate in 10 ml of ether was added to a solution of 6.24 g of 10-(diethylaminoacetyl)phenothiazine in 50 ml of anhydrous ether. A white, crystalline precipitate deposited immediately, and a layer of a thick tarry mass collected on the bottom of the flask. The precipitate was filtered, and washed with ether. The compound was obtained as a white, highly hygroscopic crystalline powder, m.p. 101-102°. Its water solutions show neutral. Yield 30-35%.

Found %: S 14.87, 15.08. $C_{20}H_{26}O_5N_2S_2$. Calculated %: S 14.62.

In its pharmacological action, 10-(diethylaminoacetal)phenothiazine dimethosulfate functions as a powerful peripheral gangliolytic agent, and has been approved (under the abbreviated name of "mephazine") for clinical testing.

10-(Diethylaminoacetyl)phenothiazine methobromide.* A solution of 2 g of "mephazine" in 5-6 ml of water was treated with an excess of saturated sodium bromide solution. The obtained precipitate was filtered, and dried. Recrystallized from a mixture (1 : 1) of alcohol and water, the methobromide melts at 105-107°. Quantitative yield.

10-(Diethylaminoacetyl)phenothiazine methonitrate* was obtained in a similar manner, by precipitation with concentrated sodium nitrate solution. The precipitate was recrystallized from a mixture (1 : 1) of alcohol and water. M.p. 183-184°.

Found %: N 10.46, 10.25. $C_{19}H_{23}O_4N_3S$. Calculated %: N 10.80.

10-(α-Bromopropionyl)phenothiazine (see [1]). A mixture of 10 g of phenothiazine and 16 g of α-bromopropionyl bromide in 100 ml of toluene was heated under reflux for 5 hours. After removal of the solvent and recrystallization from alcohol, m.p. 147-148°. Yield 8.5 g (51%).

10-(α Diethylaminopropionyl) phenothiazine (see [1]). A mixture of 17 g of α-bromopropionylphenothiazine (m.p. 147-148°) and 10 g of diethylamine in 100 ml of toluene was heated for 5 hours. The reaction product was separated from the diethylamine hydrobromide by filtration. After removal of the solvent at room temperature, and recrystallization from alcohol, we obtained 12.1 g (75.6%) of product. M.p. 100-101°.

10-(α-Diethylaminopropionyl)phenothiazine hydrochloride was obtained in nearly quantitative yield by passing dry hydrogen chloride into an ether solution of the free base. White crystalline powder, readily soluble in water and alcohol. Its solutions show neutral. M.p. 190-191°.

Found %: Cl 9.76, 9.95. $C_{19}H_{23}ON_2SCl$. Calculated %: Cl 9.82.

10-(α-Diethylaminopropionyl)phenothiazine methiodide. A solution of 3.26 g of the free base in 30 ml of alcohol was heated with excess methyl iodide (3 ml) for 3 hours under reflux. The solvent was evaporated at room temperature, and the product was washed repeatedly with ether and anhydrous alcohol to give a pale yellow powder with m.p. 90-95° (with decomp.). The compound is difficultly soluble in water (0.25-0.3%). Its solubility in alcohol is 3-4%.

Found %: I 27.25, 26.89. $C_{20}H_{25}ON_2SI$. Calculated %: I 27.13.

*It is possible to use crude "mephazine," obtained as a thick tarry mass when "diphazine" is reacted with dimethyl sulfate, to obtain the methobromide (and also the methonitrate).

10-(α-Diethylaminopropionyl)phenothiazine ethiodide. A solution of 3.26 g of the free base in 30 ml of alcohol was heated for 4 hours under reflux with excess ethyl iodide (3 ml). After removal of the solvent at room temperature, the residual mass soon crystallized, and was purified by washing with ether and anhydrous alcohol. M.p. 197-199°. Its solubility in water is about 0.3%.

Found %: I 26.22, 26.55. $C_{21}H_{27}ON_2SI$. Calculated %: I 27.02.

SUMMARY

1. 10-(Diethylaminoacetyl)phenothiazine and 10-(α-diethylaminopropionyl)phenothiazine were synthesized. Both their hydrochlorides and their quaternary ammonium salts were obtained and described.

2. All of the obtained compounds show high cholinolytic activity. 10-(Diethylaminoacetyl)phenothiazine hydrochloride, under the name of "diphazine," has found use in medical practice. 10-(Diethylaminoacetyl)-phenothiazine dimethosulfate, under the name of "mephazine," is being clinically tested.

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SYNTHESIS OF SOME ACYL DERIVATIVES OF PHENOTHIAZINE

II. DERIVATIVES OF β-DIALKYLAMINOISOBUTYRIC ACID

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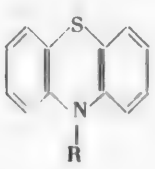
In the previous communication [1] we described a number of phenothiazine derivatives, in which the nitrogen of the phenothiazine heterocycle was linked to the diethylaminoacetyl (I) and α-diethylaminopropionyl (II) radicals.



(I) R = CO—CH_2—$N(C_2H_5)_2$,

(II) R = CO—CH(CH_3)—$N(C_2H_5)_2$,

(III) R = CO—CH(CH_3)—CH_2—$N(C_2H_5)_2$,

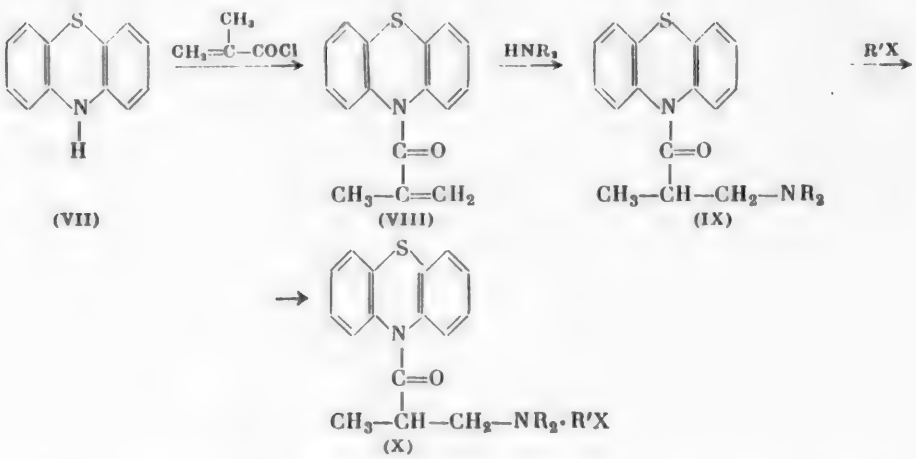
(IV) R = CO—CH(CH_3)—CH_2—$N(CH_3)_2$,

(V) R = CH_2—CH_2—$N(C_2H_5)_2$,

(VI) R = CH_3—CH(CH_3)—CH_2—$N(CH_3)_2$

In this paper we describe the synthesis and properties of phenothiazine derivatives containing the more complex acyl radicals: β-diethylaminoisobutyryl (III) and β-(N-piperidino)isobutyryl (IV), analogous to diparcol (V) and phenergan (VI), possessing valuable pharmacological properties [2].

We worked out the following synthesis path.



(VII) (VIII) (IX) (X)

As secondary amines (R_2NH) we used diethylamine and piperidine, while as the R'X to form the salts (both tertiary and quaternary) we used hydrochloric and benzoic acids, and also methyl and ethyl iodides.

10-Methacryloylphenothiazine (VIII) was obtained by heating a mixture of phenothiazine (VII) and methacryloyl chloride in benzene solution for 3 hours. Reaction of 10-methacryloylphenothiazine (VIII) with a secondary amine (either diethylamine or piperidine) gave us either 10-(β-diethylaminoisobutyryl)phenothiazine or 10[β-(N-piperidino)isobutyryl]phenothiazine (IX). The obtained bases, being liquids that slowly crystallized, were converted to the corresponding salts (X).

The obtained compounds were tested pharmacologically by E. A. Spalva. Some of them proved to be highly active local anesthetics.

EXPERIMENTAL

Methacryloyl chloride was obtained by a modification of the method described in the literature [3]. A mixture of 43 g (0.5 mole) of methacrylic acid, vacuum distilled from copper powder, and thionyl chloride, taken in 10% excess, was heated on the water bath, under reflux, for about 4 hours at 50-60°, and then for another 4 hours at 70-80°. The obtained clear liquid was distilled twice. B.p. 98-100°. Yield 70-75%.

10-Methacryloylphenothiazine (VIII). A mixture of 20 g of phenothiazine (0.1 mole) and 12 g of methacryloyl chloride (10% excess) in 200 ml of benzene was heated on a water bath, under reflux, for 3 hours. Removal of the solvent (in the air, at room temperature) left 26 g of crude product. After recrystallization from alcohol, we obtained 20.5 g of the compound. M.p. 121-122°.

Found %: C 72.17, 71.83; H 5.21, 5.11; N 5.54, 5.39. $C_{16}H_{13}ONS$. Calculated %: C 71.91; H 4.90; N 5.24.

10-(β-Diethylaminoisobutyryl)phenothiazine (IX, R = C_2H_5). A mixture of 5.34 g (0.02 mole) of 10-methacryloylphenothiazine (m.p. 121-122°) and excess diethylamine (10 ml) was heated carefully in a small flask, fitted with an efficient reflux condenser, for 2 hours, until all of the substance had dissolved, and then it was heated for another 2 hours. Removal of the excess diethylamine left a thick dark-green liquid, insoluble in water, and readily soluble in alcohol and ether. The product was purified by dissolving in ether, and then heating on the water bath under reflux, in the presence of activated carbon. The ether solution was filtered, and the ether was removed. We obtained a viscous light-green mass, which could not be made to crystallize. Yield 4.9 g (70%).

10-(β-Diethylaminoisobutyryl)phenothiazine hydrochloride. The hydrochloride was obtained in nearly quantitative yield by passing dry HCl into an ether solution of 10-(β-diethylaminoisobutyryl)phenothiazine. Here we obtained a bluish-white crystalline powder, difficultly soluble in cold water (0.3%), and more soluble in hot water. M.p. 105-107° (from alcohol).

Found %: C 63.80, 64.04; H 6.69, 6.55; N 7.32, 7.21; Cl 9.30, 9.24. $C_{20}H_{25}ON_2SCl$. Calculated %: C 63.73; H 6.69; N 7.43; Cl 9.40.

10-(β-Diethylaminoisobutyryl)phenothiazine methiodide. A solution of 3.4 g (0.01 mole) of the free base in 30 ml of ether was treated with excess methyl iodide (2 ml). Here a pale yellow finely crystalline substance separated, which was slightly soluble in water (0.3%), and readily soluble in alcohol. M.p. 206-208° (with decomp.). Yield 3.6 g (77%).

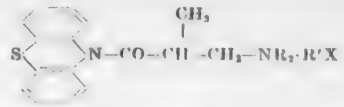
Found %: C 52.06, 52.16; H 5.59, 5.48; N 6.01, 5.93; I 26.2, 25.9. $C_{21}H_{27}ON_2SI$. Calculated %: C 52.37; H 5.65; N 5.82; I 26.34.

10-(β-Diethylaminoisobutyryl)phenothiazine ethiodide was obtained by heating 10-(β-diethylaminoisobutyryl)phenothiazine in ethyl acetate with excess ethyl iodide for 3 hours. Removal of the solvent left a tarry mass, which when rubbed with ether for a long time was converted to an amorphous yellow powder. M.p. 57-58° (with decomp.) (from aqueous alcohol).

10-(β-Diethylaminoisobutyryl)phenothiazine dimethosulfate. A solution of 1.4 g of dimethyl sulfate in 15 ml of ether was added to a solution of 3.4 g (0.01 mole) of the free base in 20 ml of dry ether. The mixtute heated up strongly. A thick, sticky mass was obtained on cooling. The compound was purified by washing with ether, and then by refluxing an ether solution of the compound with activated carbon for 10-15 min. Long drying in a vacuum desiccator gave 2.6 g of a clear, glassy, noncrystallizing mass, readily soluble in water.

10-(β-Diethylaminoisobutyryl)phenothiazine methobromide. A solution of 1.3 g of the dimethosulfate in 2 ml of water was treated in drops with a saturated solution of sodium bromide (excess). A copious precipitate

Derivatives of 10-(β-Dialkylaminoisobutyryl)phenothiazine



Expt. No.	NR_2	R'X	Melting point	Solubility in water (in %)
1	$-N(C_2H_5)_2$	—	Semiliquid	—
2	$-N(C_2H_5)_2$	HCl	105—107°	0.3
3	$-N(C_2H_5)_2$	CH_3I	206—208	0.3
4	$-N(C_2H_5)_2$	C_2H_5I	57—58	0.3
5	$-N(C_2H_5)_2$	$CH_3SO_4CH_3$	Semiliquid	50
6	$-N(C_2H_5)_2$	CH_3Br	148—150°	0.3—0.4
7	$-N(C_2H_5)_2$	CH_3NO_3	178—181	0.4—0.5
8	$-N(C_2H_5)_2$	C_6H_5COOH	95—97	1
9	$-N(CH_2)_5$	—	106—108	—
10	$-N(CH_2)_5$	HCl	232—234	0.25
11	$-N(CH_2)_5$	CH_3I	220—222	0.25—0.3
12	$-N(CH_2)_5$	C_2H_5I	70—72	0.3
13	$-N(CH_2)_5$	C_6H_5COOH	102	1

was formed. The dried product was recrystallized from aqueous alcohol. M.p. 148-150°. Yield nearly quantitative.

Found %: Br 18.23, 18.28. $C_{21}H_{27}ON_2SBr$. Calculated %: Br 18.39.

10-(β-Diethylaminoisobutyryl)phenothiazine methonitrate. An excess of saturated $NaNO_3$ solution was added to a solution of 1.3 g of the dimethosulfate in 2 ml of water. A copious precipitate was obtained, which was filtered, washed with water, and dried. M.p. 178-181° (from aqueous alcohol). Nearly quantitative yield. The compound was obtained as a finely crystalline white powder with a pink tinge, difficultly soluble in water (about 0.5%).

Found %: C 60.27, 60.46; H 6.18, 6.29; N 10.15, 9.96. $C_{21}H_{27}O_4N_3S$. Calculated %: C 60.43; H 6.52; N 10.07.

10-(β-Diethylaminoisobutyryl)phenothiazine benzoate. A solution of 0.34 g (0.01 mole) of 10-(β-diethylaminoisobutyryl)phenothiazine in 3 ml of alcohol was filtered, and the filtrate was treated with a solution of 0.12 g of benzoic acid in 2 ml of alcohol. Removal of the solvent at room temperature left a green sticky mass, which solidified in the vacuum desiccator. M.p. 95-97°. Yield 0.25 g. Green crystalline powder, soluble in alcohol. Its solubility in water is about 1%.

10-[β-(N-Piperidino)isobutyryl]phenothiazine. A mixture of 5.34 g (0.02 mole) of 10-methacryloylphenothiazine and 6 ml of piperidine in 30 ml of toluene was heated for 4 hours under reflux. Removal of the solvent left a thick green mass, which changed to a green powder when dried in a vacuum desiccator. M.p. 106-108° (from alcohol). Yield 4.2 g (60%).

10-[β-(N-piperidino)isobutyryl]phenothiazine hydrochloride. The salt was obtained in nearly quantitative yield by passing HCl into an ether solution of the 10-β-piperidinoisobutyrylphenothiazine. M.p. 232-234° (from aqueous alcohol). The salt is slightly soluble in cold water, and readily soluble in hot water and in alcohol.

Found %: C 64.92, 64.75; H 6.83, 6.66; N 7.38, 7.33; Cl 9.13, 9.08. $C_{21}H_{25}ON_2SCl$. Calculated %: C 64.86; H 6.48; N 7.20; Cl 9.13.

10-[β-(N-Piperidino)isobutyryl]phenothiazine methiodide. A solution of 3.52 g (0.01 mole) of the 10-β-piperidinoisobutyrylphenothiazine in 30 ml of ether was treated with excess methyl iodide at room temperature. The precipitate was filtered, repeatedly washed with ether, and dried carefully. M.p. 220-222° (from aqueous alcohol). Yield 3.6 g (72%).

Found %: C 53.60, 53.22; H 5.68, 5.62; N 5.89, 5.59; I 25.36, 25.75. $C_{22}H_{27}ON_2SI$. Calculated %: C 53.44; H 5.50; N 5.66; I 25.70.

10-[β-(N-Piperidino)isobutyryl]phenothiazine ethiodide. A solution of 2.5 g (0.02 mole) of the free base in 20 ml of ethyl acetate was treated with excess ethyl iodide (2 ml). The mixture was heated for 1 hour under reflux. The tarry precipitate turned to a powder when rubbed with ether for some time; the product was purified by washing with ether. M.p. 70-72° (with decomp.). Yield 1.9 g (53%).

Found %: C 54.58, 54.27; H 5.98, 6.03; N 5.82, 5.04; I 25.10, 25.6. $C_{23}H_{29}ON_2SI$. Calculated %: C 54.33; H 5.75; N 5.51; I 25.00.

10-[β-(N-Piperidino)isobutyryl]phenothiazine benzoate. A solution of 0.35 g (0.01 mole) of the free base in 3 ml of alcohol was filtered, and the filtrate was mixed with a solution of 0.12 g of benzoic acid in 1 ml of alcohol. Removal of the solvent left a thick mass, which crystallized in the vacuum desiccator. Finely crystalline gray-green powder. M.p. 102°. Readily soluble in alcohol, acetone, and ethyl acetate, and insoluble in ether. Solubility in water 1%.

SUMMARY

1. 10-Methacryloylphenothiazine was synthesized.

2. A method was developed for the preparation of 10-(β-dialkylaminoisobutyryl)phenothiazines by reacting 10-methacryloylphenothiazine with secondary amines.

3. Thirteen new derivatives of 10-(β-diethylaminoisobutyryl)phenothiazine and 10-[β-(N-piperidino)isobutyryl]phenothiazine were obtained.

4. Some of the synthesized compounds show both local anesthetic and cholinolytic properties.

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STUDY OF THE NATURE OF CARBON – METAL BONDS BY THE ISOTOPIC EXCHANGE METHOD

I. EXCHANGE OF ETHYL GROUPS

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The isotopic exchange method, first used by von Hevesy [1] in the domain of organometallic compounds, was used chiefly to study the exchange of the central atom (for example, lead in tetraphenyllead [1] or tetraethyllead [2], or mercury in organomercury compounds [3]), or of the peripheral halogen atoms in partially filled organometallic compounds [4].

In contrast to the above indicated directions, in [5] the exchange of diphenylmercury and deuterated benzene was studied, as well as that of phenylmercury hydroxide and benzene. This work was repeated [6], but using C^{14}-labeled benzene, in which connection the conclusions of the previous work were confirmed. As a result, the exchange of hydrocarbon radicals was studied only in the last two papers.

The exchange of dissimilar radicals, for example, methyl and ethyl or phenyl, was studied in a number of papers [7] without using radioactive isotopes, while the exchange of ethyl and chlorine in the system $(C_2H_5)_4Pb$ + + $(C_2H_5)_3PbCl$ was studied using labeled lead (RaD) [8], but the exchange of the same radicals between organometallic compounds with different metals has not been studied at all. In addition, it is specifically such exchange that offers information as to the comparative stability of the C–Me bond for different metals.

In this paper we studied the exchange of ethyl groups between the organometallic compounds of mercury, lead, sodium, magnesium, zinc, and aluminum. The results of the study are given in the table. In most cases the exchange is accompanied by partial decomposition of the compound, which at times is quite substantial, and for this reason the percent of exchange bears a tentative value: changes in the molar ratios of the compounds were neglected in calculating it.

The table shows that in systems, containing tetraethyllead, the exchange goes poorly, with the exception of system 8 (tetraethyllead + triethylaluminum). In systems, containing diethylmercury, the exchange goes much better, especially in cases 2 and 4 (diethylmercury + ethylmagnesium bromide or triethylaluminum). In the last case there is no visible evidence of decomposition. In general, it should be mentioned that decomposition is much less in systems containing diethylmercury than in systems containing tetraethyllead. Consequently, the instability of the bond and the ability to exchange do not run parallel.

It is interesting to mention that triethylaluminum readily exchanges ethyl groups with both diethylmercury and tetraethyllead, and in this case steric hindrance, which could be used to explain the poor exchange shown by tetraethyllead, plays little part.

EXPERIMENTAL

1) Ethyl bromide, labeled with C^{14}, was synthesized by the earlier described procedure [9]. The compound had an activity of 7.6 mC/mole. For the exchange reactions, a part of it was diluted to 160.8 μ C/mole.

Expt. No.	System and molar ratios of the compounds	Experimental conditions	Original activity of labeled compound (in μ C/mole)	Activity of 1st component after experiment		Exchange (in %)	Remarks
				(in μC / mole)	(in % of original activity)		
1	Diethylmercury + C^{14}-labeled ethylsodium (1 : 2)	Room temperature, 2.5 mo.,	231.7	22.0	4.75	9.5	Sealed ampul
		100°, 5 hr.	220.7	43.9	9.95	19.9	Open system under nitrogen
2	Diethylmercury + C^{14}-labeled ethylmagnesium bromide (1 : 1)	100°, 5 hr. in ether	160.8	79.8	49.4	74.1	Small amount of precipitate obtained
3	C^{14}-labeled diethylmercury + + diethylzinc (2 : 3)	65°, 20 hrs.	463.4	386.3	83.4	27.7	Small amount of precipitate obtained
4	Diethylmercury + C^{14}-labeled triethylaluminum (2 : 1)	100°, 5 hrs.	109.2	18.6	34.0	59.5	External appearance of the mixture unchanged
5	Tetraethyllead + C^{14}-labeled diethylmercury (1 : 1)	100°, 20 hrs.	463.4	None	None	None	Precipitate obtained
6	Tetraethyllead + C^{14}-labeled ethylsodium (1 : 2)	Room temperature, 2.5 mo.	231.7	2.85	0.6	0.9	Profound decomposition
7	Tetraethyllead + C^{14}-labeled ethylmagnesium bromide (1 : 1)	100°, 5 hr, in ether	160.8	6.4	4.0	5.0	Precipitate obtained
8	Tetraethyllead + C^{14}-labeled triethylaluminum (2 : 1)	100°, 5 hrs.	109.2	16.3	29.8	41.0	Small amount of precipitate obtained

2) Diethylmercury, labeled with C^{14} in both ethyl groups, was synthesized from labeled ethyl bromide (diluted 12 times) and 0.5% sodium amalgam by the method [10] developed for nonradioactive mercury, and had an activity of 463.4 μ C/mole.

3) Ethylsodium, labeled with C^{14}, was synthesized from labeled diethylmercury using the method of [11] (for nonradioactive ethylsodium).

4) Triethylaluminum was obtained from labeled diethylmercury and aluminum shavings by the method of Buckton and Odling (for nonradioactive triethylaluminum), described in the monograph [12]. The activity of the triethylaluminum (109.2 μ C/mole) was determined by calculation, proceeding from the activity of the labeled diethylmercury.

All of the compounds (both labeled and unlabeled) used in our study were purified carefully, and had constants that agreed with those given in the literature.

For the most part, the exchange experiments were run in sealed glass ampuls. Prior to experiment, the ampul was heated in a drying oven, and then blown with nitrogen until completely cold. Maintaining a constant stream of nitrogen, the compounds were introduced into the ampuls in amounts of 0.01 to several g-mole, but always in the taken molar ratio. Solvents were not used, except in the experiments with organomagnesium compounds, which were run in ether solution.

After introducing the compounds, the ampuls were sealed under nitrogen. The heating was done in an air thermostat. The ampuls were opened under nitrogen, the unstable organometallic compounds decomposed with either water or wet nitrogen, while the second component of the mixture was extracted with a suitable solvent, dried, the solvent distilled off, and the compound distilled. In the case of stable organometallic compounds, the mixture was separated by fractional distillation in vacuo at the lowest possible temperature.

Combustion of the organometallic compounds in order to analyze for their activity was run by the combined method of wet oxidation and conventional combustion: the combustion tube, filled with copper oxide, was connected to an apparatus in which the wet oxidation was run. Such a procedure prevents the loss of carbon as highly volatile substances (ethane), and at the same time the metal from the organometallic compound is retained in the oxidation mixture.

The evolved carbon dioxide was trapped in saturated barium hydroxide solution. The activity of the $BaCO_3$ precipitates was measured as described earlier [13], in which connection a $BaCO_3$ specimen, obtained from the original active compound, served as a standard.

The impulses were counted with an accuracy of 1-2%. The experimental conditions and results are given in the table.

SUMMARY

1. Experiments were run to study the exchange of ethyl groups between organometallic compounds in eight systems: 1) diethylmercury–ethylsodium, 2) diethylmercury–ethylmagnesium bromide, 3) diethylmercury–diethylzinc, 4) diethylmercury–triethylaluminum, 5) diethylmercury–tetraethyllead, 6) tetraethyllead–ethylsodium, 7) tetraethyllead–ethylmagnesium bromide, and 8) tetraethyllead–triethylaluminum.

2. It was found that the exchange goes better for the more stable diethylmercury than for the less stable tetraethyllead, where the influence of steric hindrance can be postulated. The exchange goes well in the systems diethylmercury–triethylaluminum and tetraethyllead–triethylaluminum. Steric hindrance does not play a part in the last case.

Using the method of exchanging similar radicals, we have only begun to study the character of carbon–metal bonds. The work will be continued.

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HEAT EFFECT OF THE SULFONATION OF XYLENES AND ETHYLBENZENE

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The problem of the heat effect in the sulfonation of aromatic compounds is discussed in the literature on the examples of naphthalene [1] and resorcinol [2]. We determined the heat effect of the sulfonation of all of the xylene isomers and ethylbenzene.

EXPERIMENTAL

The xylene isomers and ethylbenzene used in the experiments had the following constants (Table 1).

TABLE 1

Isomers	d_4^{20}	n_D^{20}	Boiling point (760 mm)	Freezing point
m-Xylene	0.8648	1.4972	139.03°	—48.1°
p-Xylene	0.8615	1.4960	138.31	+13.02
o-Xylene	0.8805	1.5047	144.31	—25.30
Ethylbenzene	0.8662	1.4960	136.10	

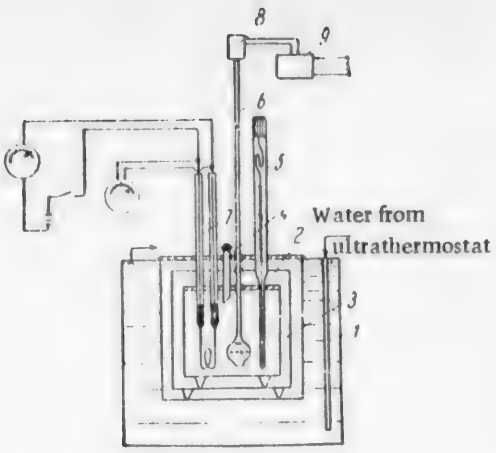
The sulfonations were run with 96.5% sulfuric acid; here the reaction was quite rapid, and the evolution of heat lasted 8-10 minutes.

The experiments were run in a calorimeter with an isothermal jacket 1 (see Fig.) at 20°. Water from an ultrathermostat was circulated through the jacket. A second jacket, a nickel-plated brass beaker 2, was contained inside the water jacket, and a glass beaker 3, serving as the reaction vessel, was placed inside the brass beaker. The reaction vessel was fitted with a Beckmann thermometer 5, an efficient stirrer 6, and a mercury electric heater 7. The stirrer was driven by electric motor 8, which was connected through a voltage regulator 9 to assure a constant stirring speed.

Sulfonation of xylene isomers. A known weight of sulfuric acid was placed in the glass beaker. After a constant temperature had been established, the heat value of the system was determined by passing a constant current through the mercury electric heater for a given length of time. The heat value K of the system was calculated in conventional manner. Corrections for radiation in determining the heat value of the system in the sulfonation experiments were made using the Regnault-Pfaundler equation [3].

The system was brought to the initial temperature, held there until a constant temperature had been established, and then a known weight of hydrocarbon, having the same temperature as the sulfuric acid in the reaction vessel, was introduced through tube 4. The rise in temperature was measured, making suitable correction for radiation. The heat value K of the system was redetermined at the end of experiment. Usually it differed from the initial value (prior to experiment) by 0.3-0.5%. The average value of K was used in calculating the heat effect of the sulfonation reaction.

To calculate the heat effect ΔH of the reaction, we used the equation



Calorimeter for determining the heats of sulfonation. Explanation in text.

$$\Delta H = \frac{K \cdot \Delta t^{\circ} \cdot 106}{g} \text{ kcal/g-mole}$$

where K is the heat value of the system in kcal/°C, Δt° is the temperature rise in the calorimeter (with suitable correction), 106 is the molecular weight of the isomeric xylenes and ethylbenzene, and g is the weight of hydrocarbon in grams.

The results of the experiments on determining the heat effects incurred in the sulfonation of the isomeric xylenes and ethylbenzene are given in Table 2.

Since a large excess (300-3000-fold) of sulfuric acid was taken for the experiments, the change in its concentration during experiment was insignificantly small. Consequently, the obtained heat effect is a differential effect for the given concentration of sulfuric acid. The heat effect of the true sulfonation reaction is obtained by subtracting the differential heat of sulfuric acid dilution from the experimentally obtained total heat effect. The value of the differential heat effect of sulfuric acid dilution was obtained from Brönsted's data [4].

TABLE 2

Expt. No.	Weight (in g)		Heat value of system (kcal/-/°C)	Temp. rise (with suitable correction)	Total heat effect (kcal/g-mole)		Heat effect (in kcal/g-mole)	
	sulfuric acid	hydrocarbon			ΔH	ΔH_{av}	of sulfuric acid dilution	of sulfonation reaction
				m-Xylene				
1	486.77	1.4343	0.186	0.840°	11.55	11.46	7.61	3.9 ± 0.1
2	488.37	1.1892	0.187	0.685	11.42			
3	487.50	0.9292	0.187	0.531	11.33			
4	495.94	1.1440	0.193	0.646	11.53			
				p-Xylene				
1	470.10	1.8988	0.184	1.151	11.86	11.73	7.61	4.1 ± 0.2
2	469.25	1.2114	0.185	0.715	11.55			
3	469.00	0.8458	0.185	0.515	11.91			
4	495.05	0.8944	0.193	0.510	11.64			
5	494.50	0.9336	0.193	0.535	11.70			
				o-Xylene				
1	468.75	1.7791	0.192	1.133	12.97	13.07	7.61	5.5 ± 0.2
2	467.10	0.6512	0.192	0.432	13.38			
3	466.40	0.9900	0.192	0.626	12.87			
				Ethylbenzene				
1	466.37	0.3713	0.185	0.244	12.89	12.67	7.61	5.1 ± 0.2
2	465.90	0.1620	0.185	0.105	12.71			
3	465.65	1.1826	0.185	0.747	12.40			

From the obtained data it can be seen that the true heat effect for the sulfonation of the isomeric xylenes and ethylbenzene represents from 34 to 42% of the total heat effect of the sulfonation process.

SUMMARY

The heat effect incurred in the sulfonation of the isomeric xylenes and ethylbenzene with 96.5% sulfuric acid was determined, and the following values were obtained: m-xylene 3.9, p-xylene 4.1, o-xylene 5.5, and ethylbenzene 5.1 kcal/g-mole, respectively.

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SOME 2,2'-(POLYHYDROXYALKYLENE)DIBENZIMIDAZOLES

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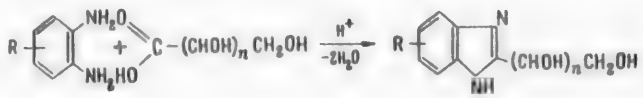
Carbon–carbon derivatives of sugars, containing heterocyclic radicals,are beginning to assume a very important place in the chemistry of carbohydrates [1].

Of great interest are the benzimidazole derivatives that find utility for the identification of aldoses, aldonic, uronic,and saccharic acids [2]. There are statements in the literature that individual compounds of this type show some carcinolytic activity [3].

Benzimidazole derivatives of carbohydrates are formed by the condensation of aromatic o-diamines with aldoses, aldonic,or saccharic acids. As had been established [4], the heating of o-phenylenediamine with a glucose in water solution gives, in small yield, both the benzimidazole compound and the quinoxaline derivative of the sugar. The highest yields of benzimidazole compounds were observed in the case where the aldose was first oxidized to the aldonic acid, and the latter was then condensed with o-phenylenediamine in the presence of mineral acid condensing agents ($ZnCl_2$, HCl, mixture of H_3PO_4 + HCl) [2, 5], by the scheme:



The condensation of saccharic acids with two moles of o-phenylenediamine yields 2,2'-(polyhydroxyalkylene)dibenzimidazoles [6].

Using the method of [2] to condense o-phenylenediamine with the dibasic saccharic acids: xylo- and L-arabotrihydroxyglutaric acids, we were able to obtain the previously unknown dibenzimidazole derivatives in good yield. The compounds were obtained as crystalline, very high melting substances forming both picrates and hydrochlorides.

In this paper we give an improved method for obtaining the compounds: 2,2'-(dihydroxyethylene)benzimidazole and 2,2'-(dihydroxyethylene)dibenzimidazole, described earlier by Hudson and co-workers [7]. We were able to increase the yields of these compounds by using a mixture of hydrochloric and orthophosphoric acids as the condensing agent, and by making some changes in the method of isolating the end products. In order to obtain more accurate analytical characterization, the indicated substances were converted to their picrates and hydrochlorides, and also the diacetyl derivative of 2,2'-(dihydroxyethylene)dibenzimidazole was prepared.

We were able to establish that some of the acetylated aldonic and saccharic acids could be identified as the benzimidazole derivatives, and here the latter were obtained in excellent yield. The conditions used for condensation with o-phenylenediamine results in complete removal of the acetyl groups, and the same products are obtained as in the reaction of the aldonic and saccharic acids themselves. Thus, tetraacetylmucic acid and its dichloride, when heated with 2 moles of o-phenylenediamine in the presence of mineral acids, yield the dibenzimidazole derivatives in 50-60% yield. In a similar manner, the condensation of the γ-lactone of tetraacetyl-D-galactonic acid with o-phenylenediamine gave 2-[(D-galacto)pentahydroxyamyl]benzimidazole in 61% yield. In all cases, together with the main products, we isolated 2-methylbenzimidazole, which is formed

as the result of the cleaved acetyl groups reacting with the o-phenylenediamine.

The obtained benzimidazole products are easily oxidized with alkaline potassium permanganate solution, giving 2-benzimidazolecarboxylic acid in good yield, which is in full agreement with the data of Huebner and co-workers [8]. The oxidation of 2,2'-(dihydroxyethylene)dibenzimidazole with sodium periodate yields 2-formylbenzimidazole in nearly quantitative yield, and the latter when oxidized with alkaline hydrogen peroxide solution is converted to 2-benzimidazole-carboxylic acid.

EXPERIMENTAL

2,2'-[(Xylo)trihydroxypropylene]dibenzimidazole. A mixture of 2.18 g (0.01 mole) of the calcium salt of xylotrihydroxylglutaric acid [9] and 2.6 g (0.025 mole) of o-phenylenediamine was prepared in a wide test tube. Then the mixture was heated with 4 ml of water, 4 ml of alcohol, 4 ml of concd. hydrochloric acid and 1.5 ml of sirupy (85%) orthophosphoric acid. The suspension was heated in an oil bath at 135-140° for 2 hr; the melt was cooled, and dissolved in hot water; the water solution was decolorized with activated carbon, and then made weakly alkaline with ammonia solution. A colorless crystalline product separated from the alkaline solution, which was filtered, washed with water, acetone, alcohol, and ether, and then air-dried. Yield 3 g (92%). The compound is practically insoluble in water, alcohol, acetone, dioxane, and the other common organic solvents. The compound was purified by repeated boiling of its hydrochloric acid solution with activated carbon, followed by precipitation with ammonia. When heated in a capillary, the substance darkens and shrivels at 260°, but does not melt up to 360°. The compound is new.

Found %: C 62.61; H 4.76; N 17.15. $C_{17}H_{16}O_3N_4$. Calculated %: C 62.96; H 4.94; N 17.28.

Picrate. A boiling suspension of 0.1 g of the above substance in 2 ml of alcohol was treated with 1 ml of a hot alcohol solution of picric acid. The solution was filtered hot. The filtrate on cooling deposited lemon-yellow leaflets. The picrate was filtered, washed with alcohol and water, and dried. M.p. 235-236° (decompn.).

2-Benzimidazolecarboxylic acid. A suspension of 1 g of 2,2'-[(xylo)trihydroxypropylene]dibenzimidazole in 30 ml of 1 N NaOH solution was treated with 1.7 g of potassium permanganate. The mixture was heated on the boiling water bath for 30 minutes. Then 1 ml of alcohol was added, the manganese dioxide was filtered, and the filtrate was acidified with dilute hydrochloric acid. Cooling gave colorless crystals, which were filtered, and dried. Yield 0.38 g (38%). After recrystallization from aqueous alcohol, m.p. 168-169° (decompn.). When heated in an oil bath for 10 minutes at 200° the acid decarboxylates completely, yielding benzimidazole. After recrystallization from water, m.p. 170°. The mixture melting point with authentic benzimidazole was not depressed. The picrate was obtained as yellow needles with m.p. 222-223°.

2,2'-[(L-Arabo)trihydroxypropylene]dibenzimidazole. The condensation product was obtained by evaporating a mixture of 1.25 g (0.0057 mole) of potassium arabotrihydroxyglutarate [10], 1.51 g (0.014 mole) of o-phenylenediamine, 2.5 ml of water, 3 ml of alcohol, 3 ml of concd. hydrochloric acid and 1.5 ml of orthophosphoric acid to a sirup , and then working up the sirup as described above. Yield 1.3 g (70%). The compound darkens when heated above 225°, and decomposes, without melting, when heated above 350°. Oxidation of the compound with alkaline potassium permanganate solution gave 2-benzimidazolecarboxylic acid.

Found %: C 62.63; H 4.73; N 17.14. $C_{17}H_{16}O_5N_4$. Calculated %: C 62.96; H 4.94; N 17.28.

The picrate was obtained from an alcohol solution as lemon-yellow leaflets. The substance charred above 360° when its melting point was taken.

2,2'-(Tetrahydroxybutylene)dibenzimidazole. a) The compound was obtained from a mixture of 3.78 g (0.01 mole) of tetraacetylmucic acid [11], 2.28 g (0.021 mole) of o-phenylenediamine, 4 ml of alcohol, 4 ml of water, 3 ml of concd. hydrochloric acid and 2 ml of 85% orthophosphoric acid. Yield 1.95 g (55%). M.p. 295° (decompn.). From the literature [6]: m.p. 298° (decompn.). The mixed melting point with the dibenzimidazole product, obtained from mucic acid and o-phenylenediamine, was not depressed.

Found %: N 15.69, 15.76. $C_{18}H_{18}O_4N_4$. Calculated %: N 15.81.

The picrate was obtained from aqueous alcohol solution as lemon-yellow crystals, melting with decomposition at 248°. From the literature [6]: m.p. 250° (decompn.). Dilution of the acetone solution with water gave 2-methylbenzimidazole, with m.p. 173-174°, not depressing the melting point when mixed with an authentic specimen.

The oxidation of 0.7 g of 2,2'-(tetrahydroxybutylene)dibenzimidazole with alkaline potassium permanganate solution gave 0.4 g (63%) of 2-benzimidazolecarboxylic acid.

b) The dibenzimidazole product was synthesized from 4.15 g (0.01 mole) of tetraacetylmucyl dichloride [12] 3.12 g (0.03 mole) of o-phenylenediamine, 3 ml of alcohol, 4 ml of water, 4 ml of concd. hydrochloric acid and 2 ml of orthophosphoric acid. Yield 2.1 g (60%). M.p. 295° (decompn.).

Picrate, m.p. 248-249°.

Found %: N 15.87. $C_{18}H_{13}O_4N_4$. Calculated %: N 15.81.

2-[(D-Galacto)pentahydroxyamyl]benzimidazole. We obtained 1.63 g (61%) of the compound from 3.46 g (0.01 mole) of the tetraacetylgalactonic acid lactone [13], 1.2 g (0.011) mole) of o-phenylenediamine, 4 ml of water, 2 ml of alcohol, 2 ml of concd. hydrochloric acid and 1.5 ml of orthophosphoric acid. After recrystallization from water, m.p. 239-240° (decompn.). From the literature [2]: m.p. 245° (decompn.). The mixed melting point with authentic 2-[(D-galacto)pentahydroxyamyl]benzimidazole was 244° (decompn.).

Found %: N 10.32, 10.41. $C_{12}H_{16}O_5N_2$. Calculated %: N 10.48.

The picrate melted at 215° (decompn.). From the literature [2]: m.p. 217° (decompn.).

2-(Dihydroxyethylene)benzimidazole. To 1.9 g (0.019 mole) of glyceric acid, obtained from 3.2 g of barium glycerate [14], was added 2.7 g (0.025 mole) of o-phenylenediamine, 3 ml of water, 3 ml of alcohol, 3 ml of concd. hydrochloric acid, and 1.5 ml of orthophosphoric acid. After heating the mixture in an oil bath, colorless needles were obtained when the aqueous ammoniacal solution was treated with an equal volume of acetone and the solution allowed to stand in ice overnight. The product was filtered, washed with acetone and ether, and dried in a thermostat at 100-110°. The yield was 1.5 g (47%). M.p. 182-184° (decompn.) from the literature [7]: m.p. 184-186° (decompn.).

Found %: C 53.71; H 5.43; N 15.53. $C_9H_{10}O_2N_2$. Calculated %: C 53.84; H 5.49; N 15.39.

The compound is readily soluble in water, slightly soluble in alcohols, and insoluble in acetone and ether. Treatment of its water solution with solutions of either copper or silver salts gives water-insoluble colored complexes.

The picrate is formed when the compound is heated with picric acid in a small amount of water: yellow crystals with m.p. 269-270° (from water).

The hydrochloride was obtained by adding a drop of concd. hydrochloric acid and an equal volume of acetone to a suspension of the compound in alcohol. Colorless crystals, which did not melt up to 350°, and began to sublime at 250°.

Found %: Cl 16.39, 16.42. $C_9H_{11}O_2N_2Cl$. Calculated %: Cl 16.25.

2,2'-(Dihydroxyethylene)dibenzimidazole. The condensation in the usual manner of 3 g (0.02 mole) of tartaric acid with 5.2 g (0.05 mole) of o-phenylenediamine in the presence of 5 ml of water, 3 ml of alcohol, 5 ml of hydrochloric acid and 2 ml of orthophosphoric acid gave 4.5 g (77%) of a colorless crystalline product. Two recrystallizations from alcohol gave crystals that shriveled and turned dark at 260°, but did not melt up to 340°. The compound is soluble in pyridine and hot alcohol (1 g in 25 ml), but is insoluble in acetone and chloroform.

Found %: C 65.12, 65.28; H 4.59, 4.67; N 18.65. $C_{16}H_{14}O_2N_4$. Calculated %: C 65.30; H 4.76; N 19.04.

Picrate. An equal volume of a 50% alcohol solution of picric acid was added to an alcohol solution of the compound. Heating the mixture led to precipitation of the picrate, which was filtered, washed, and dried. Lustrous golden-yellow needles with m.p. 241-242° (decompn.).

Hydrochloride. The compound (0.1 g) was heated with 6 ml of alcohol and a drop of concd. hydrochloric acid until complete solution was obtained. The cooled solution was treated with an equal volume of acetone, and the crystals obtained on cooling were filtered, washed with acetone, and dried. M.p. 266-267° (decompn.). From the literature [7]: m.p. 270° (decompn.).

Found %: Cl 19.17, 19.25. $C_{16}H_{16}O_2N_4Cl_2$. Calculated %: Cl 19.34.

Diacetate. A solution of 1 g of the compound in 5 ml of dry pyridine was treated with 5 ml of acetic anhydride. After standing for two days, the solution was poured into water. The crystalline product was filtered, washed with water, and recrystallized from aqueous alcohol. Yield 0.75 g (55%). M.p. 233-234° (decompn.).

Found %: N 13.72, 12.80. $C_{20}H_{20}O_6N_4$. Calculated %: N 14.00.

2-Benzimidazolecarboxaldehyde. To a suspension of 1 g (0.0032 mole) of 2,2'-(dihydroxyethylene)dibenzimidazole in 40 ml of 1 N sulfuric acid solution was added 0.68 g (0.0032 mole) of sodium metaperiodate. The mixture was allowed to stand overnight, diluted with water, and neutralized with sodium bicarbonate. The obtained white crystalline product was filtered, washed with water, and dried. Yield 0.94 g (98%). M.p. 235° (decompn.).

The dinitrophenylhydrazone, obtained from aqueous-alcohol hydrochloric acid solution, melted at 309-311°. The oxime, obtained by heating the aldehyde with hydroxylamine hydrochloride and potassium carbonate in water solution, had m.p. 213-215°. The melting points of the aldehyde and its derivatives are in complete agreement with those given in the literature.

To a suspension of 0.5 g of 2-benzimidazolecarboxaldehyde in 15 ml of water was added 2 ml of 30% hydrogen peroxide and 8 ml of 2 N NaOH solution. The mixture was kept at room temperature for 2 hours, and then it was heated for 30 minutes on the boiling water bath. The solution was cooled and acidified with dilute hydrochloric acid. The crystals of 2-benzimidazolecarboxylic acid were filtered, and dried. Yield 0.35 g (64%). After recrystallization from aqueous alcohol, m.p. 169-170° (decompn.). The acid was converted to benzimidazole when decarboxylated at 200°.

Oxidation of 1 g of 2,2'-(dihydroxyethylene)dibenzimidazole with 1.3 g of potassium permanganate in 30 ml of 1 N NaOH solution (method described above) gave 0.54 g (50%) of 2-benzimidazolecarboxylic acid. M.p. 168-169°. Oxidation of 0.8 g of the product under the same conditions with alkaline barium permanganate solution gave 0.4 g (42%) of the acid.

SUMMARY

1. The condensation of o-phenylenediamine with xylo- and L-arabotrihydroxyglutaric acids gave previously unknown 2,2'-(trihydroxypropylene)dibenzimidazoles.

2. The methods for the preparation of 2-(dihydroxyethylene)benzimidazole and 2,2'-(dihydroxyethylene)-dibenzimidazole were improved. The previously unknown hydrochlorides and picrates, and the acetyl derivatives of the latter of these compounds, were obtained.

3. It was shown that when the γ-lactone of tetraacetylgalactonic acid, tetraacetylmucic acid, and the dichloride of the latter, are reacted with o-phenylenediamine, the C—C substituted benzimidazole derivatives of sugars are obtained in good yields. Here 2-methylbenzimidazole was isolated as a secondary product.

4. Oxidation of the obtained products with alkaline potassium permanganate solution gave 2-benzimidazolecarboxylic acid. Oxidation of 2,2'-(dihydroxyethylene)dibenzimidazole with sodium periodate gave 2-benzimidazolecarboxaldehyde in high yields.

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N-SUBSTITUTED AMIDES OF SALICYLIC ACID AND ITS DERIVATIVES

I. ARYLIDES OF 3,5-DICHLOROSALICYLIC AND 5-NITROSALICYLIC ACIDS

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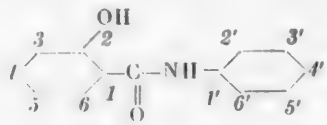
Some arylides of salicylic acid are strong disinfectants [1]. Thus, 5,3',4'-trichlorosalicylanilide ("anabial") inhibits the growth of Staphylococcus aureus at a dilution of 1 : 8,600,000.



The parent compound of this group of substances, salicylanilide, was synthesized by several routes. One of them is the condensation of salicylamide with bromobenzene in the presence of sodium acetate and finely divided copper [2, 3]. Other methods, having more practical value, are based on the reaction of salicylic acid or its derivatives with aniline. The reaction of salicylic acid with aniline goes smoothly if the mixture of these substances is heated in an inert solvent in the presence of phosphorus trichloride [4-5]. The condensation of aniline with previously prepared salicyloyl chloride is also described [7]. The condensation of aniline with esters of salicylic acid, for example, with salol [8], deserves special consideration. Phenol is liberated when salol is heated with aniline.

This "salol" method is recommended [9], as a general method for obtaining various arylides of salicylic acid by heating salol with the proper amine [10] in an inert solvent, for example, trichlorobenzene. However, our investigations revealed that it is unnecessary to use a solvent in running this reaction; to the contrary, the use of a solvent only complicates the process and leads, in the final analysis, to a reduction in the yield of arylamide. The indicated reaction goes very smoothly if the mixture of equimolar amounts of salol and amine is fused at 150-180°, in which connection the low-melting salol functions are solvent at the start of reaction, and then this function is assumed by the liberated phenol. On completion of reaction (1 to 2 hours), the phenol can be removed either by distillation or by washing with hot water, after which the obtained arylamide is purified by precipitation from alkaline solution with acid, followed by recrystallization from either alcohol or acetic acid. Using this extremely simple method we obtained, in yields ranging from 80 to 95%, not only salicylamide itself, but also other arylides of salicylic acid, and specifically, the p-anisidide [8], p-phenetidide [9], o-nitroanilide [4], m-nitroanilide [1], p-nitroanilide [11], and the α-pyridylamide [9].

This same method was also used by us to obtain derivatives of salicylanilide containing substituents in the salicyloyl ring. Here the derivatives of the chlorosalicylic acids first drew our attention.

Different chloro derivatives of salicylanilide were obtained by the chlorination of this compound [12, 13], in which connection the degree of chlorination depended on the reaction conditions used. However, a mixture of compounds is formed in all cases, differing both in the number of chlorine atoms introduced and in their position.

Thus, for example, from the mixture of substances obtained in the chlorination of salicylanilide with sulfuryl chloride, there were isolated [14] 5-chlorosalicylanilide, 5,4'-dichlorosalicylanilide and 3,5,2',4'-tetrachlorosalicylanilide.

To identify these compounds, and also to obtain other chloro derivatives of salicylanilide, containing chlorine atoms in definite positions of either the salicyloyl or arylamide groupings, the technique was used for condensing [12, 14] either salicylic acid or the chlorosalicylic acids either with aniline or with the chloroanilines in an inert solvent, using phosphorus trichloride as the condensing agent.

Our observations revealed that various pure chloro derivatives of salicylanilide are obtained smoothly by the fusion of either salol or the chlorosalols either with aniline or with the chloroanilines. In this manner we obtained 4'-chlorosalicylanilide and 2',5'-dichlorosalicylanilide [9] from salol, and 3,5,4'-trichlorosalicylanilide and 3,5,2',5'-tetrachlorosalicylanilide [1] from 3,5-dichlorosalol.

Further, by the fusion of 3,5-dichlorosalol with various amines, we obtained the corresponding 3,5-dichlorosalicylanilide derivatives, containing substituents in the arylamide grouping (Table 1). In a similar manner, by the fusion of 5-nitrosalol with various amines, we obtained the arylides of 5-nitrosalicylic acid (Table 2).

Some of the compounds in Table 2 were obtained [15] recently from 5-nitrosalicylic acid by the technique of heating the acid with the proper amine in the presence of phosphorus trichloride. However, even in this case, the "salol" method possesses certain advantages, both as regards the preparation, and especially, as regards the purification of the obtained arylides; the latter were obtained by us apparently purer, and with higher melting points than those reported in the literature [15].

EXPERIMENTAL*

Arylides of 3,5-dichlorosalicylic acid. Into a flask, fitted with reflux condenser (air) and thermometer, the latter reaching to the bottom, were charged 14.2 g of 3,5-dichlorosalol and an equimolar amount of the amine. The mixture was melted with moderate heating, and then it was heated at 150° for 2 hours (in the case of the nitroanilines the temperature of the medium was gradually raised to 180°, and kept there for 6 hours). The reaction mixture gradually thickens, and solidifies when the temperature is lowered. At the end of reaction, the still hot melt was poured into 100 ml of water, while the residue in the flask was washed several times with hot water, after which the liberated phenol was steam-distilled. The obtained residue was filtered, and washed with water until the odor of phenol had disappeared. The yield of crude reaction product was close to quantitative. The obtained precipitate was purified by dissolving in 300 ml of hot 0.2 N NaOH solution, and the arylide was precipitated from the filtered solution by the addition of dilute acetic acid. The obtained precipitate was filtered, washed with water, and dried. Final purification of the compound can be effected by recrystallization from either dilute alcohol or acetic acid. As a rule, all of the arylides of 3,5-dichlorosalicylic acid, with the exception of those containing the nitro group, show a strong violet fluorescence, and are less soluble than the corresponding arylides of salicylic acid. The properties of the obtained compounds are listed in Table 1.

Arylides of 5-nitrosalicylic acid. A mixture of 13 g of 5-nitrosalol and an equimolar amount of the amine was fused at 150-180° for 2 hours, after which the obtained mixture was worked up as described above.

The arylides of 5-nitrosalicylic acid are soluble in alkalies to give either yellow or orange solutions. On acidification, the arylides deposit either as pale yellow or faintly violet precipitates. In contrast to the arylides of salicylic and 3,5-dichlorosalicylic acids, the arylides of 5-nitrosalicylic acid do not show fluorescence either in the solid state or in solutions. When reduced, the arylides of 5-nitrosalicylic acid are converted to the corresponding arylides of 5-aminosalicylic acid, which can then be diazotized, and form azo dyes with azo components. The properties of the 5-nitrosalicylic acid arylides obtained by us are listed in Table 2.

SUMMARY

On comparing different methods for the preparation of salicylic acid arylides it was established that the most convenient for this purpose is the direct fusion of salol with amines. This method also proved suitable for obtaining the arylides of 3,5-dichlorosalicylic and 5-nitrosalicylic acids.

* With the assistance of I. Ya. Toktaeva and A. T. D'yakonova.

TABLE 1

Arylides of 3,5-Dichlorosalicylic Acid

Arylide grouping	Color	Melting point	Amount of Cl (in %)	
			calculated	found
Anilide	White	135°	25.17	24.92, 25.25
4'-Chloroanilide	Likewise	190—191	33.61	33.89, 33.99
2',5'-Dichloroanilide	"	151—152	40.4	39.86, 40.05
4-Hydroxyanilide	"	184	23.82	23.72, 24.17
4'-Methoxyanilide	"	173—174	22.71	22.55, 22.56
4'-Ethoxyanilide	"	140	21.75	21.76, 21.87
2'-Methoxyanilide	"	163—164	22.71	22.41, 22.23
2'-Methoxy-4'-chloroanilide	"	184—185	30.6	30.17, 29.94
2'-Nitroanilide	Bright yellow*	207—208	21.74	21.42, 21.97
3'-Nitroanilide	Light yellow	227—228	21.74	21.60, 21.28
4'-Nitroanilide	Yellow	> 300	21.74	21.37, 22.06
α-Pyridylamide [16]	Light yellow	182	25.09	24.83, 24.72

* Alkaline solutions have a bright orange color; the sodium salt crystallizes as orange crystals.

TABLE 2

Anilides of 5-Nitrosalicylic Acid

Anilide grouping	Color	Melting point	Amount of N (in %)		Amount of Cl (in %)	
			calculated	found	calculated	found
Anilide	Pink	221—224°	10.85	11.00, 11.21	—	—
4'-Chloroanilide	Cream	255—257	9.57	9.79, 9.40	12.14	12.18, 12.37
2',5'-Dichloroanilide	Gray	257—260	8.56	8.97, 9.19	21.67	21.29, 21.36
4'-Hydroxyanilide	Dark purple	250—254	10.22	10.29, 10.24	—	—
4'-Methoxyanilide	Green	188—190	9.68	10.10, 10.07	—	—
4'-Ethoxyanilide	Violet	200—202	9.27	9.38, 9.51	—	—
2'-Methoxyanilide	White	239—240	9.68	9.90, 10.12	—	—
2'-Methoxy-4'-chloroanilide	Yellow-green	254—256	8.68	8.59, 8.71	11.01	11.34, 11.13
2'-Nitroanilide	Yellow	198—200	13.80	14.00, 14.20	—	—
3'-Nitroanilide	Violet	230—281	13.80	13.90, 14.3	—	—
4'-Nitroanilide	Yellow	298—300	13.80	14.30, 14.20	—	—
α-Pyridylanilide	Yellow-green	260—265	16.20	16.56, 16.48	—	—

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REACTION OF 2,4,5-TRICHLOROPHENOL WITH FORMALDEHYDE

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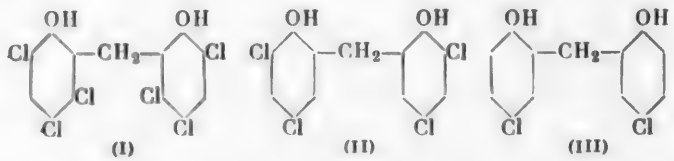
Chloro derivatives of dihydroxydiphenylmethane, containing hydroxyl groups ortho to the central methylene group, are powerful disinfectants [1]. They are far superior in this respect to the chlorophenols, and also to the chloro derivatives of dihydroxydiphenylmethane, containing hydroxyl groups in the para position.

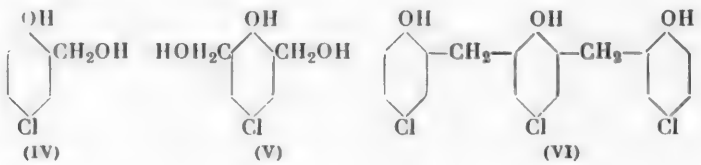
The most effective is 2,2'-dihydroxy-3,5,6,3',5',6'-hexachlorodiphenylmethane (I), supplied under the tentative name of "G-11," and called hexachlorophene for short. It is obtained by the condensation of formaldehyde with 2,4,5-trichlorophenol [2]. However, the conditions under which this condensation is run are inadequately described in the literature.



(I) (II) (III)

More detailed data exist for the related compounds (II) and (III), obtained from formaldehyde and either 2,4-dichlorophenol or 4-chlorophenol. The reaction of these chlorophenols with formaldehyde proceeds in conventional manner [3]: the primary condensation products are methylol derivatives, which, depending on the reaction conditions, can suffer further transformations, leading to the formation of the dihydroxydiphenylmethane derivatives, as well as of other compounds.

From 4-chlorophenol, having two positions ortho to the hydroxyl group open, it is possible to obtain as intermediate product both the monomethylol derivative, chlorosalicyl alcohol or chlorosaligenin (IV), and the dimethylol (with excess formaldehyde) derivative, 2,6-dimethylol-4-chlorophenol (V).

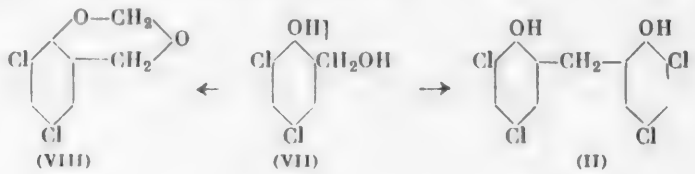


(IV) (V) (VI)

The condensation of chlorosaligenin (IV) with excess 4-chlorophenol yields 2,2'-dihydroxy-4,4'-dichlorodiphenylmethane (III). In like manner, the condensation of 2,6-dimethylol-4-chlorophenol (V) with excess 4-chlorophenol yields the more complex reaction product (VI).

Compounds (III) and (VI), in which the terminal benzene rings have the positions ortho to the hydroxyl groups open, are capable of reacting further with formaldehyde to yield higher molecular weight compounds. For this reason, the condensation of 4-chlorophenol with formaldehyde leads to the formation of a mixture of products, from which only a small amount of 2,2'-dihydroxy-4,4'-dichlorodiphenylmethane (III) can be isolated [4].

The reaction of formaldehyde with 2,4-dichlorophenol was studied in detail by Ziegler [5]. In this reaction the primary product is the methylol derivative, dichlorosaligenin (VII), which can be isolated if the reaction is run in an alkaline medium; in the presence of acids, even dilute, the first formed dichlorosaligenin reacts further either with formaldehyde to yield the cyclic methylene ether (VIII), or with 2,4-dichlorophenol to yield 2,2'-dihydroxy-3,5,3',5'-tetrachlorodiphenylmethane (II).



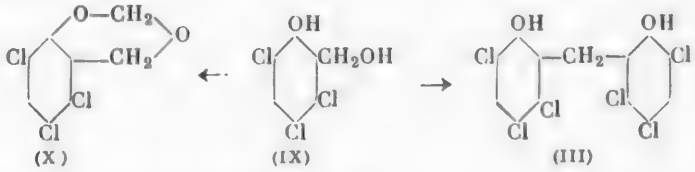
It could be expected that the condensation of formaldehyde with 2,4,5-trichlorophenol, similar to 2,4-dichlorophenol, having a position ortho to the hydroxyl group open, would go in a similar manner. However, it was shown experimentally that when 2,4,5-trichlorophenol is reacted with formaldehyde, under conditions sufficient to effect the condensation of formaldehyde with 2,4-dichlorophenol, the 2,4,5-trichlorophenol fails to react and is recovered unchanged from the reaction mixture.

On studying the properties of 2,4,5-trichlorophenol it was found that it, in contrast to 2,4-dichlorophenol, is also quite inactive in other substitution reactions. It is not sulfonated with concentrated sulfuric acid at 100-120°, it fails to react with the nitrating mixture when nitrated under the conditions usually used for the nitration of phenols, and it practically does not react with bromine. 2,4,5-Trichlorophenol also does not react with formaldehyde in alkaline medium, i.e., under the conditions usually used to obtain methylol derivatives of phenols. For 2,4,5-trichlorophenol to be so inactive in substitution reactions, despite the presence of an open position ortho to the hydroxyl group, is possibly due to the steric hindrance exerted by the chlorine in the 5 position.

In a series of comparative experiments it was established that it is possible to effect the condensation of 2,4,5-trichlorophenol with formaldehyde only under comparatively drastic conditions, in the presence of concentrated sulfuric acid at 90-100°. Here, together with the known hexachlorophene [2], which melts at 161-162°, and is soluble in alkali, a second product is formed, which melts at 112°, and is insoluble in alkali. Analysis revealed that the latter is the previously unknown methylene ether of trichlorosaligenin [X].

The proportions of the two condensation products, hexachlorophene and the trichlorosaligenin methylene ether, depend on the reaction conditions. If a small amount of sulfuric acid is added to a mixture of formaldehyde (better as paraform) and the trichlorophenol, heated to 100°, then the sole reaction product is the trichlorosaligenin methylene ether in up to 30% yield; here up to 70% of the original trichlorophenol is recovered unchanged. When a mixture of formaldehyde and concentrated sulfuric acid is added to a hot mixture of the trichlorophenol in sulfuric acid the main reaction product is hexachlorophene, the yield of which reaches 75-80%; however, even under these conditions about 5% of the trichlorosaligenin methylene ether is formed, and there also remains some unreacted trichlorophenol. The hexachlorophene was purified through the monosodium salt.

It could be assumed that the primary reaction product in the condensation of formaldehyde with 2,4,5-trichlorophenol is also the methylol derivative – trichlorosaligenin (IX), which, in view of the low chemical activity of the trichlorophenol, is formed only in the presence of concentrated sulfuric acid at 90-100°. However, under these conditions, the compound, possessing a methylol group, is more reactive and reacts immediately either with formaldehyde, or with excess starting trichlorophenol.



In view of the low activity of the trichlorophenol, the reaction of the methylol derivative with formaldehyde proceeds at the more rapid rate. For this reason, when excess formaldehyde is present in the reaction mixture, the

main reaction product is the trichlorosaligenin methylene ether (X). Only with an excess of the trichlorophenol, and with a longer time of heating in the presence of substantial amounts of concentrated sulfuric acid, is hexachlorophene (III) formed, which, under these conditions, is the main, but not the sole, reaction product.

As a result, although the reaction of formaldehyde with 2,4,5-trichlorophenol proceeds formally by the same scheme as in the case of 2,4-dichlorophenol, still this reaction, due to the specific characteristics of 2,4,5-trichlorophenol, proceeds with some deviations.

In studying the properties of hexachlorophene, we prepared its monosodium salt, as well as the diacetyl and dibenzoyl derivatives.

EXPERIMENTAL*

Trichlorosaligenin methylene ether. Three milliliters of concentrated sulfuric acid was added with stirring to a molten mixture of 20 g of 2,4,5-trichlorophenol and 5 g of paraform, heated to 100°; some rise in the temperature of the mixture was observed. The mixture was heated for another 10 minutes, and then the hot melt was poured into water. The rapidly solidifying mass was filtered, washed several times with water, and then treated with 10% NaOH solution under heating. Acidification of the combined alkaline solutions with dilute sulfuric acid gave 13.5 g of an oily product, which solidified on cooling, and melted at 56-58° (the starting 2,4,5-trichlorophenol had m.p. 58-59°). The alkali insoluble solid product was recrystallized twice from alcohol. Colorless crystals, m.p. 111-112°.

Found %: Cl 44.55, 44.18. $C_8H_5O_2Cl_3$. Calculated %: Cl 44.47.

2,2'-Dihydroxy-3,5,6,3',5',6'-hexachlorodiphenylmethane. a) To 100 g of molten 2,4,5-trichlorophenol was added 50 ml of concd. H_2SO_4 with stirring. Then to the mixture, heated on the water bath, was added in drops, with stirring, in 1 hour, a mixture of 30 ml of 30% formalin and 100 ml of concd. H_2SO_4, after which the stirring, with heating at 80-90°, was continued for another 3 hours. The hot reaction mixture was poured with good stirring into 1 liter of cold water. The obtained precipitate was filtered, repeatedly washed with hot water, and then dissolved with heating in 300 ml of 10% NaOH solution. Here about 5 g of alkali insoluble substance remained in the precipitate, which after recrystallization from alcohol had m.p. 111-112°, and was the above described trichlorosaligenin methylene ether.

The alkaline filtrate was treated with 25 ml of 50% sulfuric acid, and then carbon dioxide was passed through the solution for 1 hour until it showed weakly alkaline (to phenolphthalein). Here the precipitate was the monosodium salt of hexachlorophene, difficultly soluble in water (0.25%), and even less soluble in the presence of carbonates or bicarbonates. The 2,4,5-trichlorophenol remained in solution. The hexachlorophene monosodium salt was filtered, washed several times with water, and then transferred to a beaker with 500 ml of hot water. Then 10% sulfuric acid was added with good stirring until acid (to Congo). The obtained precipitate was separated, washed thoroughly, and dried. Total yield of hexachlorophene 80 g (77.3%). M.p. 156-158°; after recrystallization from alcohol, m.p. 161-162°.

Found %: Cl 52.46, 52.51. $C_{13}H_6O_2Cl_6$. Calculated %: Cl 52.33.

Hexachlorophene is difficultly soluble in water, and is readily soluble in ammonia and alkali solutions (depending on the amounts of the latter either the monometallic or dimetallic salts are formed). The compound remains unchanged when heated with concd. sulfuric acid to 120°, and also when heated with potassium bisulfate above 200°. Only when treated with concd. sulfuric acid at 160-180° does hexachlorophene go into solution, and here the strong odor of the trichlorophenol appears, which indicates decomposition of the hexachlorophene.

b) Monosodium salt. The monosodium salt of hexachlorophene is difficultly soluble in cold water, much more soluble in hot water, and on cooling separates from solution as long, colorless, threadlike crystals, which fact can be utilized for purification. When washed with water the monosodium salt hydrolyzes partially, leading to a low sodium analysis.

Found %: Na 4.89, 4.86. $C_{13}H_5O_2Cl_6Na$. Calculated %: Na 5.36.

* With the assistance of A. T. D'yakonova.

c) Diacetyl derivative. Ten grams of hexachlorophene was dissolved in 30 ml of acetic anhydride in the presence of 2 ml of concd. sulfuric acid, and the mixture refluxed for 2 hours. The mixture was then poured into water to give a white precipitate, which was separated, washed, and dried. Yield 11 g (87.4%). After recrystallization from alcohol, m.p. 175-176°. Readily soluble in hot acetic acid.

Found %: Cl 43.32, 43.28. $C_{17}H_{10}O_4Cl_6$. Calculated %: Cl 43.38.

d) Dibenzoyl derivative of hexachlorophene. To a solution of 10 g of hexachlorophene in 100 ml of 0.5 N NaOH was added, with stirring, 8 g (10% excess) of benzoyl chloride. An oil layer collected on the bottom of the flask, which congealed on cooling. The precipitate was separated, washed, and dried. Yield 15 g (99.9%). The compound in soluble in both hot alcohol and benzene. It suffers partial hydrolysis in aqueous alcohol to yield the monobenzoyl derivative. After recrystallization from alcohol, m.p. 172-173°.

SUMMARY

2,4,5-Trichlorophenol condenses with formaldehyde only when heated in the presence of concentrated sulfuric acid. Here 2,4,5-trichlorosaligenin is formed as the intermediate product, which then condenses further either with excess formaldehyde or with excess 2,4,5-trichlorophenol, to give in the first case the cyclic methylene ether of 2,4,5-trichlorosaligenin, and 2,2'-dihydroxy-3,5,6,3',5',6'-hexachlorodiphenylmethane (hexachlorophene) in the second case. Both the diacetyl and dibenzoyl derivatives of hexachlorophene were prepared.

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REFORMATSKII REACTION WITH α-HALONITRILES

IV. CONDENSATION OF KETONES WITH BROMOACETONITRILE

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In previous communications [1] we described the reaction of bromoacetonitrile with various aromatic aldehydes, run under conventional Reformatskii conditions, and leading to the formation of β-hydroxynitriles. Continuing to study this reaction, we condensed various ketones (acetophenone, cyclohexanone and dibutyl ketone) with bromoacetonitrile and obtained the corresponding β-hydroxynitriles. Partial dehydration occurs when β-hydroxy-β-phenylbutyronitrile is distilled, yielding β-methylcinnamonitrile as impurity. The hydroxynitrile can be isolated from the higher boiling fraction by recrystallization. The pure unsaturated nitrile was obtained by dehydrating the mixture of nitriles with potassium bisulfate.

The solvent used exerts an influence on the reaction course. When bromoacetonitrile was reacted with acetophenone, it was established that running the reaction in benzene, toluene, or a mixture of benzene and ether, yields predominantly tarry products; in dioxane, ether, or their mixture, the yields of nitriles do not exceed 38.5%; the best results (67.8% yield) were obtained using tetrahydrofuran as the solvent (Table 1). The previously unknown nitriles, except for 5-hydroxy-5-cyanomethylnonane, were converted to the corresponding amides, and in addition, β-methylcinnamonitrile was converted to β-methylcinnamic acid.

TABLE 1

Influence of Solvent on the Course of the Reformatskii Reaction Between Bromoacetonitrile and Acetophenone

Solvent	Amount (in ml)	Yield of nitrile (in %)	Recovered acetophenone (in g)
Dioxane	50	*	4.65
Dioxane + ether	40 + 10	*	3.65
Ether	15	38.5 **	2.1
Tetrahydrofuran	25	67.8 **	1.23

*A mixture of hydroxynitrile and unsaturated nitrile was obtained.

**Dehydrated with $KHSO_4$ to β-methylcinnamonitrile.

EXPERIMENTAL

In all cases the Reformatskii reaction was run with 0.1 g-mole of the ketone, 0.12 g-mole of bromoacetonitrile, 8 g of zinc turnings and 0.3 g of mercuric chloride in 25 ml of tetrahydrofuran (except, for the experiments in which the influence of the solvent, was studied, given in Table 1).* The experimental results are summarized in Table 2, while the properties of the amides are given in Table 3.

*For the method of operation, purification of the zinc, preparation of the bromoacetonitrile, and conversion of the nitriles to the amides, see [1].

TABLE 2

Starting ketone	Obtained nitrile	Boiling point (pressure in mm)	Yield (in %)	Melting point	Formula	Calculated (in %)			Found (in %)		
						C	H	N	C	H	N
Acetophenone*	β-Methylcinnamonitrile	111—131° (4) **	—	—		—	—	—	—	—	—
	β-Hydroxy-β-phenyl-butyronitrile	131—148° (4) **	—	61° (from CCl_4)	$C_{10}H_{11}ON$	74.50	6.87	8.69	74.6	6.72	8.77
Acetophenone	β-Methylcinnamo-nitrile***	90—94° (1.5)	67.8	Liquid	$C_{10}H_9N$	83.88	6.33	9.78	83.57	6.15	9.39
Cyclohexanone*	1-Hydroxy-1-cyano-methylcyclohexane	105—110° (2)	70	Liquid****	$C_8H_{13}ON$	69.06	9.36	10.08	68.54	9.10	9.81
Dibutyl ketone*****	5-Hydroxy-5-cyano-methylnonane	111—114° (2)	26.5	Liquid	$C_{11}H_{21}ON$	72.07	11.55	7.64	72.05	11.80	7.69

* Technical products were used, dried over $MgSO_4$, and distilled.

** Pure compounds could not be obtained by distillation.

*** The 129-180° (4 mm) fraction (10.68 g) was heated with 3 g of $KHSO_4$ for 5 hours at 160-180°, then extracted with benzene, and distilled, $n^{20}D$ 1.5783, d^{20}_{20} 1.0333.

**** $n^{24}D$ 1.4805, the value given in the literature [2] is $n^{25}D$ 1.4796.

***** Obtained by the pyrolysis of calcium valerate, yield 56%, b.p. 86-88° (24 mm).

TABLE 3

Compound	Yield (in %)	Melting point	Formula	Calculated (in %)			Found (in %)		
				C	H	N	C	H	N
β-Hydroxy-β-phenyl-butyramide	72	82—82.5° (from toluene)	$C_{10}H_{13}O_2N$	67.01	7.31	7.81	66.91	7.17	7.98
β-Methylcinnamamide	19.5	122—123° (from benzene)	$C_{10}H_{11}ON$	74.50	6.87	8.69	74.78	7.08	8.71

Trans-β-methylcinnamic acid. A mixture of 0.5 g of β-methylcinnamonitrile and 20 ml of 2 N KOH solution was refluxed for 16 hours, the mixture cooled, extracted with ether, and the water layer acidified to give trans-β-methylcinnamic acid; yield 0.05 g, m.p. 98°, which corresponds to the literature data [3].

SUMMARY

1. The Reformatskii reaction between bromoacetonitrile and ketones proceeds normally, and leads to the formation of β-hydroxynitriles.

2. The nitriles of β-methylcinnamic, β-hydroxy-β-phenylbutyric and β-hydroxy-β-butylheptanoic acids were obtained.

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REFORMATSKII REACTION WITH α-HALONITRILES

V. REACTION OF BENZALDEHYDE AND ACETOPHENONE WITH CHLOROACETO-, α-BROMOPROPIO-, AND α-BROMOISOBUTYRONITRILES

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In this paper we attempted to expand the earlier described [1] Reformatskii reaction with bromoacetonitrile to other α-halonitriles: chloroacetonitrile, a-bromopropionitrile, and α-bromoisobutyronitrile. Each of these nitriles was reacted with benzaldehyde and with acetophenone. As could be assumed by analogy with the reactions of ethyl chloroacetate, chloroacetonitrile reacts with somewhat more difficulty than the corresponding bromo compound, and gives lower yields of β-hydroxynitriles, whereas the α-methyl derivatives of bromoacetonitrile (α-bromopropio- and α-bromoisobutyronitriles) react more easily than bromoacetonitrile, and give higher yields of the corresponding β-hydroxynitriles.

The same as in previous papers [1], the obtained nitriles were identified by conversion to the corresponding β-hydroxyamides. However, not all of the nitriles could be made to react here. It proved necessary to extend the time of reacting α-methyl- and α,α-dimethyl-β-hydroxy-β-phenylpropionitriles with hydrogen peroxide to 3 hours, and that of α-methyl- and α,α-dimethyl-β-hydroxy-β-phenylbutyronitriles to 6 hours. Here only the first three nitriles gave the corresponding nitriles in small yields, while rupture of the carbon chain occurred in the case of α,α-dimethyl-β-hydroxy-β-phenylbutyronitrile, resulting in the formation of acetophenone (identified as the 2,4-dinitrophenylhydrazone); a small amount of acetophenone was also formed in the case of the α-methyl-β-hydroxy-β-phenylbutyronitrile.

Hydrolysis of the nitriles(refluxing for 12 to 15 hours with KOH) failed to give the expected cinnamic acids, which is apparently due to the influence exerted by α-substituents on the stability of the carbon chain.

EXPERIMENTAL

Chloroacetonitrile. A well mixed mixture of 160 g of chloroacetamide [2] and 150 g of phosphorus pentoxide was distilled at ~300 mm; the 95-105° fraction was neutralized with dry sodium carbonate, let stand for 24 hours, filtered, and distilled a second time at atmospheric pressure to give 101 g of chloroacetonitrile; b.p. 123.5-126°. The literature [3] gives b.p. 123-124°.

α-Bromopropionitrile. To 400 ml of propionic acid and 45 g of red phosphorus was added 444 ml of bromine in 10 hours (the second half with heating on the water bath). The upper layer was separated, and then carefully treated with 240 ml of methanol, followed by washing with 2 liters of water, after which the product was distilled to give 407 g of methyl α-bromopropionate, b.p. 144-150°. The obtained ester was stirred with 250 ml of 25% aqueous ammonia at 10-15° for 3 hours, after which the product was filtered and washed with a small amount of water to give 277 g of α-bromopropionamide, m.p. 117-119° (literature [4], m.p. 123°). The dried amide was mixed well with 275 g of phosphorus pentoxide, and the mixture was heated and distilled at ~60 mm. The distillate was neutralized with dry sodium carbonate, followed by two distillations to give 155 g of α-bromopropionitrile, b.p. 52-54° (62 mm). Literature [5], b.p. 59° (24 mm).

α-Bromoisobutyronitrile. α-Bromoisobutyryl bromide [6] (222 g) was added carefully between −10 and +5° to 200 ml of 25% aqueous ammonia, after which the product was filtered, dried, and recrystallized from ethyl acetate to give 145 g of α-bromoisobutyramide, m.p. 148°. Using the procedure of [7], the amide was converted to the nitrile; yield 100 g, m.p. 133-140°.

TABLE 1

Carbonyl compound	Nitrile	Obtained product	Yield (in %)	Boiling point (pressure in mm)	Melting point	Formula	Calculated (in %)			Found (in %)		
							C	H	N	C	H	N
Benzaldehyde	Bromoaceto-nitrile	β-Hydroxy-β-Phenyl-propionitrile*	48	147—151° (4—5)	—							
Acetophenone	The same	β-Methylcinnamoni-trile*	67.8	90—94° (2)	—							
Benzaldehyde	Chloroaceto-nitrile	β-Hydroxy-β-phenyl-propionitrile	24	141—162° (4)	—		**	—	—	—	—	—
Acetophenone	The same	β-Methylcinnamo-nitrile***	44.2	99—104° (4)	—		**	—	—	—	—	—
Benzaldehyde	α-Bromo-propionitrile	β-Hydroxy-β-phenyl-α-methylpropio-nitrile	82.3	144—144.5° (4)	—	$C_{10}H_{11}ON$	74.50	6.87	8.69	74.39	6.67	8.52
Acetophenone	The same	β-Hydroxy-β-phenyl-α-methylbutyro-nitrile	77.1	136—139° (4)	—	$C_{11}H_{13}ON$	75.39	7.47	7.99	75.07	7.50	7.65
Benzaldehyde	α-Bromoiso-butyronitrile	β-Hydroxy-β-phenyl-α,α-dimethyl-propionitrile	83.7	159—164° (1.5)	77—78° **** from CCl_4	$C_{11}H_{13}ON$	75.39	7.47	7.99	75.66	7.88	7.82
Acetophenone	The same	β-Hydroxy-β-phenyl-α,α-dimethyl-butyronitrile	45.8	185—193° (1.5)	87 from CCl_4	$C_{12}H_{15}ON$	76.15	7.98	7.40	75.69	7.92	7.19

*Given for comparison, for preparation see Communications I and IV [1].

**Identified as the amide, see Table 2.

***Dehydrated by heating with $KHSO_4$.

****From the literature [8], m.p. 67-68°.

TABLE 2

Compound	Yield (in %)	Melting point	Formula	Calculated (in %)			Found (in %)			Literature data
				C	H	N	C	H	N	
β-Hydroxy-β-phenyl-propionamide	38.1	120° (from alcohol)	—	—	—	—	—	—	—	122—123° [9]
β-Methylcinnamamide	19.5	122—123° (from benzene)	$C_{10}H_{11}ON$	74.50	6.87	8.69	74.78	7.08	8.71	119° [10]
β-Hydroxy-β-phenyl-α-methylpropionamide	23.4	136.5—137° (from ethyl acetate)	$C_{10}H_{13}O_2N$	67.01	7.31	7.81	67.4	7.35	7.51	134—135° [11]
β-Hydroxy-β-phenyl-α-methylbutyramide	81.6	164—165° (from ethyl acetate)	$C_{11}H_{15}O_2N$	68.36	7.82	7.24	68.45	7.87	7.45	—
β-Hydroxy-β-phenyl-α,α-dimethyl-propionamide	88.5	134—136° (from ethyl acetate)	$C_{11}H_{15}O_2N$	68.36	7.82	7.24	68.16	7.96	7.10	—

The Reformatskii reaction was run using 0.1-g-mole of carbonyl compound and 0.12 g-mole of α-halonitrile.* The results are given in Tables 1 and 2, where, for comparison, are also given the earlier described [1] results obtained with bromoacetonitrile.

SUMMARY

1. Chloroaceto-, α-bromopropio- and α-bromoisobutyronitriles enter into Reformatskii reaction with both benzaldehyde and acetophenone, yielding the corresponding β-hydroxynitriles.

2. Branching of the chain at the α-carbon atom in β-hydroxynitriles renders their hydrolysis to β-hydroxyamides and unsaturated acids difficult.

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*The method of operation and preparation of the starting materials were described earlier [1].

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CARBYLAMINE HALIDES

III. NEW METHOD FOR PREPARATION OF CARBYLAMINE FLUORIDES

K. A. Petrov and A. A. Nelmysheva

The first representatives of the carbylamine fluorides were obtained in 1953 by the pyrolysis of tri(perfluoroalkyl)amines [1]. In 1955-1956 Haszeldine obtained trifluoromethylcarbylamine fluoride and heptafluoropropylcarbylamine fluoride by subjecting the addition products of tetrafluoroethylene with trifluoronitrosomethane and heptafluoronitrosopropane, respectively, to pyrolysis [2]. Such methods for the synthesis of carbylamine fluorides have very limited value. They permit obtaining only the perfluoroalkylcarbylamine fluorides, and cannot be used to synthesize carbylamine fluorides in which an unfluorinated radical is linked directly to the nitrogen. All of the known carbylamine fluorides are given in the table.

Starting compound	Reaction temperature and catalyst	Carbylamine fluorides	Boiling point
$CF_3-N(-O-CF_2-CF_2-O-)$	550°	$CF_3N{=}CF_2$ [2]	−34°
$(C_2F_5)_3N$	745	$C_2F_5N{=}CF_2$ [1]	13.2
$C_3F_7-N(-O-CF_2-CF_2-O-)$	550	$CF_3CF_2CF_2N{=}CF_2$ [2]	25.6
$[CF_2(CF_2)_3]_3N$	645—650	$CF_3(CF_2)_3N{=}CF_2$ [1]	39
$(C_2F_5)_3N$	500—550, $AlF_3 \cdot Al_2O_3$	$CF_3CF_2N{=}CFCF_3$ [1]	13—13.5
$(C_3F_7)_3N$	500—550, $AlF_3 \cdot Al_2O_3$	$CF_3CF_2CF_2N{=}CFCF_2CF_3$ [1]	56.5—57.5

In this paper we describe a new method for the synthesis of carbylamine fluorides, which is based on the cleavage of the elements of hydrogen fluoride from secondary amines, containing the trifluoromethyl group. As we had indicated earlier, these amines can be synthesized by the reaction of carbylamine chlorides with hydrogen fluoride [3].

Phenyltrifluoromethylamine and hexafluorodimethylamine were subjected to dehydrofluorination. Here it was shown that phenylcarbylamine fluoride is formed when trifluoromethylphenylamine is heated with potassium fluoride, in the absence of solvent, at 140-150° for 4-5 hours. Carbylamine fluoride boils at 49° (12 mm), and keeps comparatively well in a glass weighing bottle without stabilizer. Hydrogen fluoride fails to be cleaved when phenyltrifluoromethylamine is heated with quinoline, either in the presence or absence of a solvent.

Triple passage of hexafluorodimethylamine through a glass tube with a diameter of 9 mm, filled with granulated KF (length of KF layer 50 cm), and heated to 140-150°, gave trifluoromethylcarbylamine fluoride in up to 70% yield. A part of the hexafluorodimethylamine is converted to a substance that fails to distil at room temperature, which was not investigated more closely.

Attempts to obtain carbylamine fluorides by replacing the chlorine in carbylamine chlorides by fluorine, using various metal fluorides, proved unsuccessful. When phenyl- or β-chloroethylcarbylamine chloride is heated with either potassium fluoride or potassium bifluoride at 100-110° for 6-8 hours, the original carbylamine chloride is recovered unchanged. The formation of hydrogen chloride was observed when phenylcarbylamine chloride was heated with potassium bifluoride for a long time at 170-180°, but we were unable to isolate any carbylamine fluoride from the reaction mixture. It is possible that the formed carbylamine fluoride suffers decomposition under the reaction conditions.

Trifluoromethylcarbylamine fluoride boils at −32° to −33°, reacts vigorously with amines, and is easily hydrolyzed by water to CO_2, F^- and NH_4^+. In the hydrolysis of the carbylamine fluoride, the water apparently first adds to the double bond. The obtained unstable product then decomposes with the cleavage of hydrogen fluoride and the formation of the acid fluoride of trifluoromethylcarbamic acid, which then undergoes further hydrolysis.

$$CF_3N{=}CF_2 \xrightarrow{+H_2O} CF_3NHC\begin{matrix}F\\F\\OH\end{matrix} \xrightarrow{-HF} CF_3NHC\begin{matrix}O\\F\end{matrix}$$

The mechanism for the hydrolysis of trifluoromethylcarbylamine fluoride bears a resemblance to the mechanism for the hydrolysis of hexafluorodimethylamine, proposed by us earlier [3].

The hydrolysis of trifluoromethylcarbylamine fluoride was also studied by Haszeldine [4], who believes that the high reactivity of the fluorine in the difluoromethylene group plays the major role in the hydrolysis reaction, and that the primary hydrolysis product is the isocyanate. Trifluoromethyl isocyanate and hexafluorodimethylamine were isolated by Haszeldine when he ran the hydrolysis reaction in excess carbylamine fluoride. However, it should be mentioned that any of the above discussed mechanisms are equally suitable for explaining the formation of all of the intermediate and end hydrolysis products of carbylamine fluorides.

EXPERIMENTAL

Phenylcarbylamine fluoride. A mixture of 8 g of freshly prepared phenyltrifluoromethylamine and 4.5 g of powdered potassium fluoride (150% excess) was heated, with constant stirring, at a bath temperature of ~140°, for 5 hours. At the end of heating, the precipitate was separated, and washed well with ether. Weight of precipitate 4.9 g. The ether was distilled from the filtrate, and the residue was fractionated in vacuo. After two fractional distillations we isolated a substance with b.p. 55-57° (17 mm), or 49° (12 mm), d^{20}_4 1.2114, and $n^{21.5}D$ 1.4805, from the fluorine content corresponding to phenylcarbylamine fluoride.

Found %: F 26.58, 26.13. $C_7H_5NH_2$. Calculated %: F 26.97.

The amount of fluorine in the compound was determined by hydrolysis with 1 N NaOH, with heating for 1 hour, and subsequent titration of the fluorine with thorium nitrate [5]. Reaction of phenylcarbylamine fluoride with aniline yields symmetrical diphenylurea.

Trifluoromethylcarbylamine fluoride. Dehydrofluorination was effected by passing the vapors of hexafluorodimethylamine through a glass tube with an internal diameter of 9 mm, filled with granulated fused potassium fluoride to a length of 50 cm, and heated to 140-147°. Ampoules were connected to each end of the tube, one of which was kept constantly at −75° and served as the receiver, while the second ampoule served as the vaporizer. When the compound was passed a number of times through the tube, the ampoules served alternately as receiver and as vaporizer. For the first two passages of the compound through the tube, the vaporization was run at room temperature. For subsequent passages of the substance, the vaporizer was placed in a cooling mixture at −20°. In the last case the dehydrofluorination products were collected, and were no longer subjected to dehydrofluorination. The residue in the vaporizer was vaporized at room temperature, passed twice through the tube, and then added to the main dehydrofluorination product. The trifluoromethylcarbylamine fluoride was then isolated by distillation through a Podbelniak column.

The dehydrofluorination of 9 g of hexafluorodimethylamine, after distillation through a Podbelniak column, gave 6 g of substance with b.p. −32 to −33°, from the molecular weight, and amount of fluorine and carbon, corresponding to trifluoromethylcarbylamine fluoride.

Found %: C 18.45, 18.64; F 71.25, 71.06. M 131.6. C_2NF_5. Calculated %: C 18.04; F 71.43. M 133.

Trifluoromethylcarbylamine fluoride reacts with amines, and is hydrolyzed by water to CO_2, F^-, and NH_4^+.

To a solution of 3.7 g of aniline in 15 ml of absolute ether, cooled to −70°, was added 0.5 g of the carbylamine fluoride, after which the ampoule was sealed, and allowed to stand at room temperature for a day. After opening the ampoule, the precipitate was filtered, washed well with ether, then with water, sodium carbonate solution, and again with water. We obtained 0.7 g of substance, which was insoluble, even when heated, in ether, ethyl alcohol, benzene, chloroform, carbon tetrachloride, acetone, and water; m.p. 182°. The crude product was analyzed. From the amount of carbon (67.3%), hydrogen (5.03%) and fluorine (10.75%), the substance corresponds approximately to either $C_6H_5NHCF_2N{=}C(NHC_6H_5)_2$ or $[(C_6H_5NH)_3CNHNHC_6H_5] \cdot 3HF$. The same substance is obtained when aniline is reacted with hexafluorodimethylamine. The structure of the obtained anilide was not investigated more closely.

SUMMARY

A method was developed for obtaining carbylamine fluorides by the dehydrofluorination of secondary amines containing the CF_3 group, using KF and a temperature of 140-150°. The method was used to obtain phenyl- and trifluoromethylcarbylamine fluorides.

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REACTION OF ORGANOSILICON URETHANS AND ORGANOMONO-HYDROXYSILANES WITH ALCOHOLS

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In an earlier paper [1] we had shown that the reaction of trialkylhydroxysilanes with diisocyanates proceeds without the formation of by-products. Here the reaction is accompanied by migration of the hydroxyl hydrogen of the trialkylhydroxysilane to the nitrogen atom of the isocyanate group with the formation of organosilicon urethans.

$$R\begin{matrix}NCO\\NCO\end{matrix} + 2HOSiR_3 \rightarrow R\begin{matrix}NHCOOSiR_3\\NHCOOSiR_3\end{matrix}$$

It was established that organosilicon urethans are very sensitive to hydrolysis, which goes easily under the influence of water in the absence of catalysts.

$$R\begin{matrix}NHCOOSiR_3\\NHCOOSiR_3\end{matrix} + 2H_2O \rightarrow R\begin{matrix}NH_2\\NH_2\end{matrix} + 2CO_2 + 2HOSiR_3 .$$

We devote this communication to a study of the properties of organosilicon urethans. It was found that they are capable of reacting not only with water, but also with alcohols. The reaction proceeds with the formation of diamine, carbon dioxide, and trialkyl-substituted ester of orthosilicic acid. The indicated products can be formed in the following manner: the organosilicon urethan, reacting with traces of water present in the alcohol, forms the dicarbamic acid and trialkylhydroxysilane. The bicarbamic acid, being unstable, decomposes into carbon dioxide and diamine, while the trialkylhydroxysilane reacts with the alcohol to form the trialkyl-substituted ester of orthosilicic acid.

$$R\begin{matrix}NHCOOSiR'_3\\NHCOOSiR'_3\end{matrix} + 2H_2O \rightarrow \left[R\begin{matrix}NHCOOH\\NHCOOH\end{matrix}\right] + 2HOSiR'_3$$

$$\downarrow$$

$$R\begin{matrix}NH_2\\NH_2\end{matrix} + 2CO_2$$

$$R'_3SiOH + HOR'' \rightarrow R'_3SiOR'' + H_2O.$$

To confirm the indicated reaction mechanism it was necessary to determine whether trialkylhydroxysilanes could react under such conditions, i.e., in the absence of catalysts, with alcohols. Our experiments on the matter revealed that trialkylhydroxysilanes actually do react with organic alcohols, both in the presence of a diamine and in its absence, by the scheme:

$$R'_3SiOH + HOR'' \rightarrow R'_3SiOR'' + H_2O.$$

This reaction was tested on the examples of reacting triethylhydroxysilane with methyl, propyl, butyl, and isoamyl alcohols. Here new compounds were obtained, the properties of which are listed in the table.

Properties of Substituted Esters of Orthosilicic Acid of General Formula $(C_2H_5)_3SiOR$

No. of comp.	R	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR found	MR calc.
(III)	CH_3	141—142° (747)	1.4146	0.8266	44.20	45.05
(IV)	C_3H_7	173—174 (743)	1.4186	0.8197	53.70	54.30
(V)	C_4H_9	191 (745)	1.4226	0.8212	58.24	58.93
(VI)	iso-C_5H_{11}	203 (747)	1.4250	0.8212	62.88	63.56

The experimental data obtained by us confirm the mechanism given above for the reaction of organosilicon urethans with alcohols.

EXPERIMENTAL*

Reaction of toluene-2,4-dicarbamic acid, bis(triethylsilyl) ester (I) with methyl alcohol. A mixture of 43.8 g of (I) (m.p. 152-153°) and 51.2 g of methyl alcohol (b.p. 64°), previously dried over copper sulfate and then distilled, was placed in a round-bottomed flask, fitted with a reflux condenser connected to a calcium chloride tube. The flask was heated with periodic shaking in a paraffin bath at 60-80° until CO_2 evolution ceased. The reaction mixture was then allowed to cool to room temperature, and the obtained crystals were filtered, and recrystallized from alcohol. We obtained 4.7 g (38.5%) of toluene-2,4-diamine (II) with m.p. 99°.

Found %: C 69.03, 69.01; H 8.29, 8.26; N 22.81, 22.93. $C_7H_{10}N_2$. Calculated %: C 68.85; H 8.19; N 22.95.

Repeated fractional distillation of the filtrate gave 12.8 g (43.8%) of triethylmethoxysilane (III).

B.p. 141° (747 mm), d^{20}_4 0.8286, $n^{20}D$ 1.4152, MR 44.13; calc. 45.04.

Found %: C 57.77, 57.74; H 12.24, 12.26; Si 18.79, 18.96. M 140, 141. $C_7H_{18}OSi$. Calculated %: C 57.53; H 12.32; Si 19.17. M 146.

Reaction of (I) with propyl alcohol. The reaction was run at 80-100° by the method described above. For reaction we took 43.8 g of (I) and 48 g of propyl alcohol, previously dried over copper sulfate. We obtained 4.8 g (39.3%) of (II) with m.p. 99°.

Found %: C 68.85, 68.70; H 8.25, 8.26; N 22.92, 22.89. $C_7H_{10}N_2$. Calculated %: C 68.85; H 8.19; N 22.95.

Repeated fractional distillation of the filtrate gave 16.5 g (47.4%) of triethylpropoxysilane (IV).

B.p. 173° (743 mm), d^{20}_4 0.8198, $n^{20}D$ 1.4188, MR 53.6; calc. 54.3.

Found %: C 62.30, 62.31; H 12.77, 12.76; Si 15.85, 15.95. M 166, 167. $C_9H_{22}OSi$. Calculated %: C 62.06; H 12.64; Si 16.09. M 174.

Reaction of (I) with butyl alcohol. The reaction was run at 82-105° by the method described above. For reaction we took 43.8 g of (I) and 59.2 g of butyl alcohol, previously dried over copper sulfate and distilled. We obtained 6 g (49.1%) of (II) with m.p. 99°.

Found %: C 68.86, 68.83; H 8.19, 8.26; N 22.67, 22.69. $C_7H_{10}N_2$. Calculated %: C 68.85; H 8.19; N 22.95.

Repeated fractional distillation of the filtrate gave 12.2 g (32.4%) of triethylbutoxysilane (V).

B.p. 190-191° (745 mm), d^{20}_4 0.8205, $n^{20}D$ 1.4248, MR 58.56; calc. 58.93.

Found %: C 63.72, 63.92; H 12.87, 12.91; Si 14.62, 14.66. M 183, 182. $C_{10}H_{24}OSi$. Calculated %: C 63.82; H 12.76; Si 14.89. M 188.

*For brevity we have adopted the following designations below: toluene-2,4-dicarbamic acid, bis(triethylsilyl) ester (I), toluene-2,4-diamine (II), and triethylhydroxysilane (VII).

Quantitative determination of the CO_2 formed in the reaction of (I) with butyl alcohol. The reaction of (I) with butyl alcohol was run in a two-necked flask, fitted with a reflux condenser that was connected to the following apparatus: a H_2SO_4 trap, a U-shaped calcium chloride tube for drying the CO_2 formed in the reaction, two connected in series potash bulbs with concentrated KOH solution for CO_2 absorption, and a control calcium chloride tube. An inlet tube in the second neck of the flask was connected to a nitrogen cylinder. A mixture of 4.3740 g of (I) (m.p. 152-153°) and 6.32 g of butyl alcohol (b.p. 116°) was placed in the flask. The flask contents were heated in a paraffin bath at 85-105° for 10 hours. A slow stream of nitrogen was passed through the entire apparatus during the whole time of heating. The amount of CO_2 formed was determined by the total weight increase of the potash bulbs and control tube, and proved to be equal to 0.8115 g (93.2%).

Reaction of (I) with isoamyl alcohol. The reaction was run at 95-115° by the method described above. For reaction we took 43.8 g of (I) and 70.4 g of isoamyl alcohol, previously dried over copper sulfate and then distilled. We isolated 6.75 g (55.3%) of (II) with m.p. 99°.

Found %: C 68.77, 68.92; H 8.26, 8.30; N 23.10, 23.16. $C_7H_{10}N_2$. Calculated %: C 68.85; H 8.19; N 22.95.

From the filtrate by repeated fractional distillation we isolated 12.5 g (30.9%) of triethylisoamyloxysilane (VI).

B.p. 203-204° (747 mm), d^{20}_4 0.8215, $d^{20}D$ 1.4250, MR 62.88; calc. 63.56.

Found %: C 65.38, 65.57; H 12.98, 12.89; Si 13.62, 13.52. M 191, 192. $C_{11}H_{26}OSi$. Calculated %: C 65.34; H 12.87; Si 13.87. M 202.

Reaction of triethylhydroxysilane (VII) with methyl alcohol. A mixture of 99 g of (VII) [b.p. 70° (18 mm), $n^{20}D$ 1.4339] and 96 g of methyl alcohol (b.p. 64°, $n^{20}D$ 1.3322), previously dried over copper sulfate and then distilled, was placed in a round-bottomed flask, fitted with a reflux condenser connected to a calcium chloride tube. The flask was heated with periodic shaking in a paraffin bath at 60-80° for 10 hours. Then the reaction mixture was distilled through a column with an efficiency of 12 theoretical plates, protected from the atmosphere by a calcium chloride tube. We isolated 11.08 g (10.77%) of (III).

B.p. 141-142° (747 mm), d^{20}_4 0.8266, $n^{20}D$ 1.4146, MR 44.20; calc. 45.04.

Found %: C 57.68, 57.76; H 12.26, 12.28; Si 18.84, 18.94. M 142, 143. $C_7H_{18}OSi$. Calculated %: C 57.53; H 12.32; Si 19.17. M 146.

Reaction of (VII) with propyl alcohol. For reaction we took 99 g of (VII) [b.p. 70° (18 mm), $n^{20}D$ 1.4339] and 180 g of propyl alcohol (b.p. 96.8°, $n^{20}D$ 1.3287), previously dried over copper sulfate and then distilled. The reaction mixture was fractionated through a column with an efficiency of 12 theoretical plates. We isolated 47.88 g (36.7%) of (IV).

B.p. 173-174° (743 mm), d^{20}_4 0.8197, $n^{20}D$ 1.4186. MR 53.70; calc. 54.3.

Found %: C 61.80, 61.83; H 12.71, 12.74; Si 15.60, 15.55. M 172. $C_9H_{22}OSi$. Calculated %: C 62.06; H 12.64; Si 16.09. M 174.

Reaction of (VII) with butyl alcohol. Here we took 99 g of (VII) [b.p. 70° (18 mm), $n^{20}D$ 1.4345] and 222 g of butyl alcohol (b.p. 116°, $n^{20}D$ 1.4000), previously dried over copper sulfate and then distilled. The reaction mixture was fractionated through a column with an efficiency of 12 theoretical plates. We isolated 84.5 g (60.0%) of (V).

B.p. 191° (745 mm), d^{20}_4 0.8212, $n^{20}D$ 1.4226, MR 58.24; calc. 58.93.

Found %: C 63.86; 63.64; H 12.91, 12.90; Si 14.46, 14.56. M 185. $C_{10}H_{24}OSi$. Calculated %: C 63.82; H 12.76; Si 14.89. M 188.

Reaction of (VII) with isoamyl alcohol. Here we took 99 g of (VII) [b.p. 70° (18 mm), $n^{20}D$ 1.4344] and 264 g of isoamyl alcohol (b.p. 129°, $n^{20}D$ 1.4092), previously dried over copper sulfate and then distilled. The reaction mixture was fractionated through a column with an efficiency of 12 theoretical plates. We isolated 55 g (36.0%) of (VI).

B.p. 203° (747 mm), d^{20}_4 0.8212, $n^{20}D$ 1.4250, MR 62.88; calc. 63.56.

Found %: C 65.23; H 12.83, 12.85; Si 13.58, 13.63. M 199. $C_{11}H_{26}OSi$. Calculated %: C 65.34; H 12.87; Si 13.87. M 202.

SUMMARY

1. It was shown that organosilicon urethans react with organic alcohols to yield the diamine, carbon dioxide, and the trialkyl-substituted ester of orthosilicic acid. The mechanism for the reaction of organosilicon urethans with alcohols was established.

2. It was established that trialkylhydroxysilanes react with alcohols. The reaction goes in the absence of catalysts to yield trialkyl-substituted esters of orthosilicic acid and water. The new compounds: triethylmethoxysilane, triethylpropoxysilane, triethylbutoxysilane, and triethylisoamyloxysilane were obtained in this manner, and their properties characterized.

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ACYLATION OF ARYLALIPHATIC DISILOXANES

II. SYNTHESIS OF ORGANOSILICON AROMATIC KETONES AND DIFUNCTIONAL KETOCARBOXYLIC ACIDS

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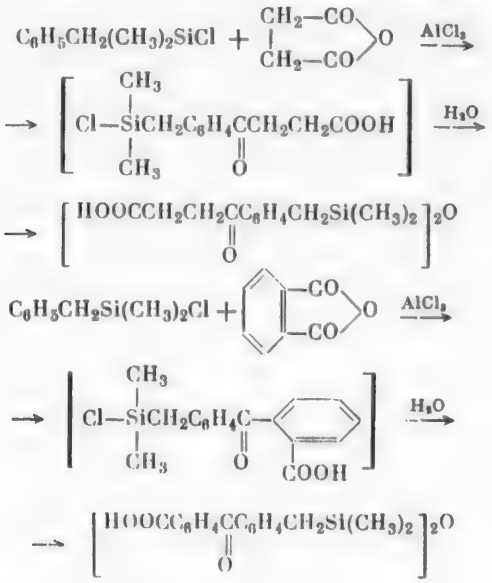
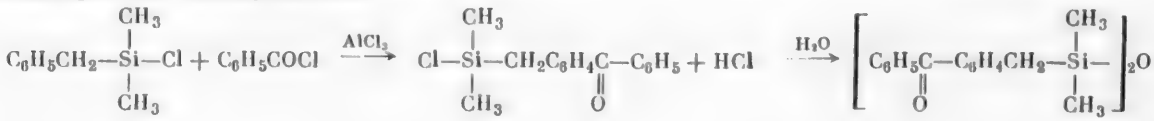
In our previous work [1] and also in the work of other investigators [2-4] the possibility of acylating benzylalkylchlorosilanes with acid anhydrides in the presence of aluminum chloride was demonstrated. As was stated previously [1], benzyldimethylchlorosilane reacts readily with acetic anhydride in the presence of aluminum chloride with the formation of bis-(4-acetobenzyl)-tetramethyldisiloxane in 50% yield.

In the present work we used this reaction to obtain organosilicon dicarboxylic acids and aromatic ketones. As subjects for the investigation, we took benzyldimethylchlorosilane and the acylating agents succinic anhydride, phthalic anhydride, and benzoyl chloride. The acylation was achieved by the following reaction scheme:



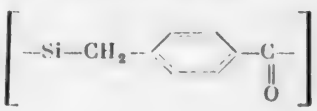
As our investigations showed, these reactions proceed smoothly in a chlorobenzene medium with a yield of silicoorganic dicarboxylic acids of 50-60%.

An aromatic diketone was synthesized by the acylation of benzyldimethylchlorosilane with benzoyl chloride according to the following equation:



Name and formula of substance	Melting point	d_4^{20}	n_D^{20}	MR found	MR calc.	% C found	% C calc.	% H found	% H calc.	% Si found	% Si calc.	COOH found	COOH calc.
Bis-[p-(α-keto-γ-carboxypropyl)-benzyl]-tetramethyldisiloxane $[HOOCCH_2CH_2\overset{\overset{O}{\|}}{C}C_6H_4CH_2Si(CH_3)_2]_2O$	149—151°	—	—	—	—	60.87, 60.92	60.67	7.13, 7.20	6.65	10.44, 10.40	10.90	16.95, 17.00	17.48
Bis-[o-carboxyphenylketobenzyl)-tetramethyldisiloxane $[HOOCC_6H_4\overset{\overset{O}{\|}}{C}C_6H_4CH_2Si(CH_3)_2]_2O$	164—166	—	—	—	—	67.62, 67.44	66.86	5.86, 5.87	5.61	9.02, 8.86	9.18	14.76, 14.75	14.73
Bis-(benzoylbenzyl)-tetramethyldisiloxane $C_6H_5\overset{\overset{O}{\|}}{C}C_6H_4CH_2Si(CH_3)_2]_2O$	B.p. 325—330 (5 mm)	1.0774	1.5720	159.62	159.42	72.46, 72.66	73.52	6.85, 6.75	6.56	10.59, 10.69	10.74	—	—
2,4-Dinitrophenylhydrazone of bis-(benzoylbenzyl)-tetramethyldisiloxane $\left[(NO_2)_2C_6H_3NHN{=}C\overset{C_6H_5}{\underset{}{}}C_6H_4CH_2\overset{CH_3}{\underset{CH_3}{Si}}\right]_2O$	235—237	—	—	—	—	59.65, 59.60	59.84	5.74, 5.86	4.79	5.70, 5.93	6.34	N 11.44, 11.42	N 12.69

This reaction gave a 40% yield of bis-(benzoylbenzyl)-tetramethyldisiloxane. Bis-(benzoylbenzyl) tetramethyldisiloxane readily formed a dinitrophenylhydrazone with m.p. 235-237°. The formation of a dinitrophenylhydrazone containing ~11.44% nitrogen was a proof of the presence of two keto groups in the molecule of the compound we synthesized.

A determination of the molecular refraction of bis-(benzoylbenzyl)-tetramethyldisiloxane showed that the molecular reaction found was 4 units higher than that calculated by Warrick's method [6]. In calculating the molecular refraction of the diketone synthesized we considered the refraction of the group  as equal to 36.77 ml/mole.*

The data obtained show that benzyldimethylchlorosilane can also be acylated with anhydrides of dicarboxylic acids and acid chlorides of monocarboxylic acids. In this case there was no noticeable destruction of either the compounds formed or those reacting under the action of the hydrogen chloride.

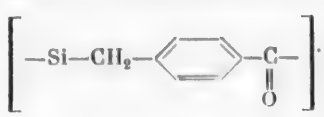
In our opinion, the application of the Friedel-Crafts reaction to benzyldimethylchlorosilane may provide a convenient method of synthesizing organosilicon polyfunctional carboxylic acids and diketones or compounds with mixed functions. The properties of the substances obtained are presented in the table.

EXPERIMENTAL

Bis-[p-(α-keto-γ-carboxypropyl)-benzyl]-tetramethyldisiloxane. Into a flask fitted with a stirrer, thermometer and reflux condenser were placed 36.9 g of benzyldimethylchlorosilane, 53.32 g of aluminum chloride and 50 ml of chlorobenzene. With vigorous stirring, 20 g of succinic anhydride was added in small portions to the mixture. When the anhydride was introduced, the temperature rose from 23 to 40° and hydrogen chloride was evolved. The introduction of the anhydride required 40 minutes. The temperature of the reaction mixture was not allowed to exceed 40°. When the succinic anhydride had been introduced, the reaction mixture was heated on a water bath at 70-80° until the evolution of hydrogen chloride ceased, and then cooled and the reaction product hydrolyzed with 20% hydrochloric acid and ice. After the hydrolysis, the chlorobenzene was steam distilled from the reaction product. The residue was treated with an aqueous solution of sodium carbonate (10.6 g), the solution filtered and the filtrate acidified with 10 ml of concentrated hydrochloric acid. The product liberated was extracted with ether, washed free from hydrochloric acid and dried with sodium sulfate and the solvent removed to yield 30.3 g of product, which had m.p. 149-151° after recrystallization from xylene. The yield was 59%.

Found %: C 60.87, 60.92; H 7.13, 7.20; Si 10.44, 10.40. $C_{26}H_{34}O_7Si_2$. Calculated %: C 60.67; H 6.65; Si 10.90.

Bis-(o-carboxyphenylketobenzyl)-tetramethyldisiloxane. Into a flask were placed 27.75 g of benzyldimethylchlorosilane, 39.9 g of aluminum chloride and 50 ml of chlorobenzene, and 22.2 g of phthalic anhydride was added in small portions with stirring. When the anhydride was introduced, the temperature rose to 35-40° and hydrogen chloride was evolved. After introduction of the phthalic anhydride, the reaction mixture was heated on a water bath at 60-70° until the evolution of hydrogen chloride ceased and the reaction product was hydrolyzed with 20% hydrochloric acid. After the hydrolysis, the chlorobenzene was steam distilled from the reaction product and the residue treated with a solution of sodium carbonate (7.42 g). The solution was filtered and the filtrate acidified with hydrochloric acid. The viscous mass precipitated was extracted with ether, washed free from hydrochloric acid, and dried with sodium sulfate. Removal of the solvent yielded 21 g of product, which had m.p. 164-166° after recrystallization from xylene. The yield was 52%.

*A. D. Petrov et al. [5] observed an increase in molecular refraction by 2 units for tetrasubstituted silanes containing one of the group  .

Found %: C 67.62, 67.44; H 5.86, 5.87; Si 9.02, 8.86. $C_{38}H_{46}O_7Si_2$. Calculated %: C 66.86; H 5.61; Si 9.18.

Bis-(benzoylbenzyl)-tetramethyldisiloxane. Into a flask were placed 26.6 g of aluminum chloride, 18.5 g of benzyldimethylchlorosilane and 50 ml of ligroine and 14 g of benzoyl chloride added to the mixture with stirring. The temperature was kept below 20°. The mixture was stirred for a further 1.5-2 hours at 50-55° until the evolution of hydrogen chloride ceased and then the reaction product was cooled and hydrolyzed with 20% hydrochloric acid with ice. After the hydrolysis, the organic layer was separated from the aqueous one, washed until neutral and dried with sodium sulfate, the solvent removed and the residue fractionated in vacuum. We obtained 10.5 g of a product with b.p. 325-330° (5 mm). The yield was 40%.

Found %: C 72.46, 72.66; H 6.85, 6.75; Si 10.59, 10.69. $C_{32}H_{34}O_3Si_2$. Calculated %: C 73.52; H 6.56; Si 10.74.

The 2,4-Dinitrophenylhydrazone of bis-(benzoylbenzyl)-tetramethyldisiloxane was obtained by a described procedure [7] by heating a mixture of solutions of 2 g of dinitrophenylhydrazine in 3 ml of concentrated sulfuric acid and 15 ml of anhydrous alcohol and 2 g of bis-(benzoylbenzyl)-tetramethyldisiloxane in 10 ml of anhydrous alcohol. The dinitrophenylhydrazone was collected and recrystallized from toluene; it had m.p. 235-237°.

Found %: C 59.65, 59.60; H 5.74, 5.86; Si 5.70, 5.93; N 11.44, 11.42. $C_{44}H_{42}O_9N_8Si_2$. Calculated %: C 59.84; H 4.79; Si 6.34; N 12.69.

SUMMARY

1. It was established that in contrast to phenylsiloxanes, organosilicon compounds with a phenyl nucleus attached to silicon through a methylene group were readily acylated with anhydrides of dicarboxylic acids to form dibasic keto acids, containing siloxane groups in the molecular chain.

2. It was shown that aromatic diketones containing siloxane groups in the molecule were readily obtained by acylation of benzyldimethylchlorosilane with benzoylchloride.

3. Bis-[p-(α-keto-γ-carboxypropyl)-benzyl]-tetramethyldisiloxane, bis-(o-carboxyphenylketobenzyl)-tetramethyldisiloxane and bis-(benzoylbenzyl)-tetramethyldisiloxane were synthesized and their properties described.

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CATALYTIC CONDENSATION OF SCHIFF'S BASES WITH ORGANIC SUBSTANCES

I. SYNTHESIS OF β-ARYLAMINO KETONES AND THEIR HYDRAMINE CLEAVAGE

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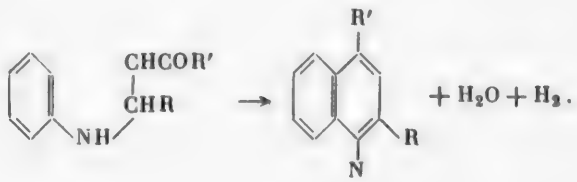
β-Amino ketones are intermediates in the synthesis of quinoline compounds [1] and substances with anesthetizing and bronchial dilating action [2]. Existing methods for their synthesis are by no means ideal and the properties of these compounds have been studied very little. The main methods for preparing β-arylamino ketones are as follows: 1) condensation of Schiff's bases with aliphatic aromatic ketones in the presence of an alcohol solution of alkali [3], 2) condensation of unsaturated aromatic ketones, chalcones, with aromatic amines [4] and 3) reaction of β-halo ketones with amines [5].

In the present work we give a description of an extremely convenient method of synthesizing β-arylamino ketones, which is based on the reaction of Schiff's bases with aliphatic aromatic ketones in the presence of an acid catalyst, namely, the hydrochloride and of the aromatic amine forming the Schiff's base. The reaction proceeds according to the following scheme:

$$ArN{=}CHAr' + RCOCH_3 \rightarrow \underset{\displaystyle CH_2COR}{\overset{\displaystyle |}{ArNHCHAr'}}.$$

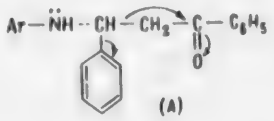
We were thus able to synthesize a series of new compounds of this class. The opinion has been expressed in the literature that β-amino ketones are readily cyclized into the corresponding quinoline bases according to the scheme [1]



We actually observed such a cyclization when Ar was β-naphthylamine. If Ar was phenyl, then under normal cyclization conditions, the β-arylamino ketone underwent hydramine cleavage [4, 6, 7]. Attempts to cyclize the β-arylamino ketones we synthesized into quinoline bases by fusion on an oil bath with zinc chloride and by heating with hydrochloric acid did not give a positive result. Heating with hydrochloric acid produced cleavage to a primary aromatic amine and benzalacetophenone.

$$\underset{\displaystyle C_6H_5}{\overset{\displaystyle |}{ArNHCHCH_2COC_6H_5}} \rightarrow ArNH_2 + C_6H_5CH{=}CHCOC_6H_5.$$

Such a course of the reaction may be explained, apparently, by the fact that the $-NH-\underset{|}{CH}-C_6H_5$ bond in the β-arylamino ketone molecule is weakened as a result of polarization in accordance with Formula (A).



(A)

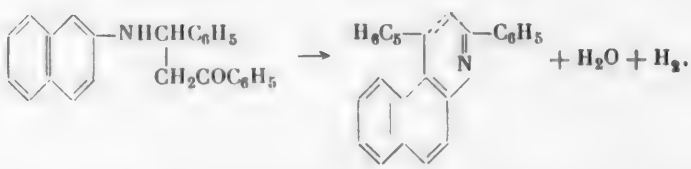
The presence of an unshared pair of electrons on the nitrogen makes the NH group nucleophilic, which facilitates the attack of a hydrogen ion. In this case a substituent on the benzene ring attached to the nitrogen must have a very strong effect on the capacity of the amino ketones to undergo cleavage. By studying the rates of hydramine cleavage of β-arylamino ketones of various structures, we were able to observe this effect, as shown by the data in Table 1.

TABLE 1

Relative Rate of Hydramine Cleavage of β-Arylamino Ketones

Name of amino ketone	Relative rate of hydramine cleavage
β-(Anilino)-β-phenylpropiophenone	100
β-(p-Toluidino)-β-phenylpropiophenone	24.4
β-(m-Toluidino)-β-phenylpropiophenone	51.0
β-(p-Nitroaniline)-β-phenylpropiophenone	72.0
β-(m-Nitroanilino)-β-phenylpropiophenone	126.0

β-(β-Naphthylamino)-β-phenylpropiophenone was cyclized into 2,4-diphenyl-5,6-benzoquinoline.



This reaction opened up a new route to the synthesis of 5,6-benzoquinoline derivatives.

EXPERIMENTAL

Synthesis of β-arylamino ketones. Equimolecular amounts of Schiff's base and acetophenone (0.05 mole) in alcohol solution with 1-2 g of the amine hydrochloride were heated on a water bath for 20-30 minutes. On cooling, the reaction product precipitated in a crystalline form and was treated with ammonia and recrystallized from alcohol or toluene to remove traces of catalyst. The following Schiff's bases were reacted with acetophenone: benzylideneaniline, benzal-p-toluidine, benzal-m-toluidine, benzal-p-anisidine, benzal-m-nitroaniline, benzal-p-nitroaniline and benzylidene-2-naphthylamine. The compounds obtained are presented in Table 2.

Hydramine cleavage of β-arylamino ketones. 0.5 g of β-anilino-β-phenylpropiophenone and 3 ml of concentrated hydrochloric acid were heated in a test tube on a boiling water bath. After a few minutes, a layer of a clear, mobile oil floated on the surface of the acid. Further heating did not produce any noticeable change. The test tube was cooled and at this the oil crystallized, and the acid solution was separated from the crystals (m.p. 56-57° after recrystallization from alcohol). A mixed melting point of the substance obtained with benzalacetophenone was not depressed. The acid solution was neutralized with alkali and the drops of oil liberated extracted with ether. After removal of the ether, the residue was treated with benzoyl chloride to yield benzanilide with m.p. 162°. No other products were detected.

TABLE 2

Name and formula of substance	Melting point		Yield (in %)	Nitrogen content (in %)	
	found	according to literature data		found	calc.
β-Anilino-β-phenylpropiophenone $C_{21}H_{19}ON$	171—172°	173°	31.3	—	—
β-(p-Toluidino)-β-phenylpropiophenone $C_{22}H_{21}ON$	172	172	24.2	—	—
β-(m-Toluidino)-β-phenylpropiophenone $C_{22}H_{21}ON$	134	—	37.5	4.65, 4.75	4.46
β-(p-anisidino)-β-phenylpropiophenone $C_{22}H_{21}O_2N$	149	—	23.5	4.33, 4.31	4.24
β-(m-Nitroanilino)-β-phenylpropiophenone $C_{21}H_{18}O_3N_2$	145	—	39.3	8.29, 8.22	8.09
β-(p-Nitroanilino)-β-phenylpropiophenone $C_{21}H_{18}O_3N_2$	185	—	29.5	8.34, 8.32	8.09
β-(2-Naphthylamino)-β-phenylpropiophenone $C_{25}H_{21}ON$	199	199	50.0	—	—

Under the same conditions, β-(p-toluidino)-β-phenylpropiophenone yielded p-toluidine with m.p. 46° and benzalacetophenone and β-(m-toluidino)-β-phenylpropiophenone gave m-toluidine and benzalacetone. When heated under analogous conditions, β-(m-nitroanilino)-β-phenylpropiophenone yielded benzalacetophenone and m-nitroaniline with m.p. 114°, β-(p-nitroanilino)-β-phenylpropiophenone gave p-nitroaniline with m.p. 146° and benzalacetophenone, and β-(p-anisidino)-β-phenylpropiophenone gave p-anisidine with m.p. 57° and benzalacetophenone.

The process of hydramine cleavage of β-aryl-β-phenylpropiophenones may be followed by the rate of conversion of the crystalline amino ketone into benzalacetophenone, which appears as a mobile oil in the hot state.

A 0.1 g sample of β-amino ketone was heated in a test tube on a water bath with 3 ml of concentrated HCl; the time for complete conversion of the original crystalline substance into a liquid product was considered the time for complete hydramine cleavage (Table 1).

Cyclization of β-(2-naphthylamino)-β-phenylpropiophenone into 2,4-diphenyl-5,6-benzoquinoline. 1 g of β-(2-naphthylamino)-β-phenylpropiophenone was heated with 5 ml of conc. HCl on a water bath for 15 minutes. The reaction mass was then made alkaline. The product liberated was recrystallized from toluene; m.p. 145°. The yield was 0.53 g (56.3%). The melting point agreed with literature data for 2,4-diphenyl-5,6-benzoquinoline [8]. A mixed melting point of the product obtained with authentic 2,4-diphenyl-5,6-benzoquinoline was not depressed.

Picrate: m.p. 231°.

SUMMARY

1. A study was made of the synthesis of β-anilino-β-phenylpropiophenone and its derivatives by the condensation of Schiff's bases with acetophenone in the presence of a catalyst consisting of the hydrochloride of the amine forming the Schiff's base.

2. A study was made of the hydramine cleavage of β-arylamino ketones when heated with hydrochloric acid to form aromatic amines and benzalacetophenone.

3. β-(2-Naphthylamino)-β-phenylpropiophenone was converted into 2,4-diphenyl-5,6-benzoquinoline when heated with hydrochloric acid.

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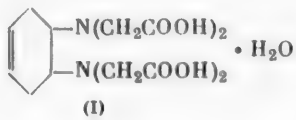
SUBSTANCES WITH COMPLEX-FORMING CAPACITY

IV. TRANS-1,2-DIAMINOCYCLOHEXENE AND 1-PHENYLETHYLENEDIAMINE-N,N,N',N'-TETRAACETIC ACID

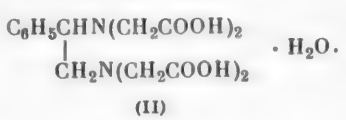
V. G. Yashunskii, V. F. Vasil'eva, L. I. Tikhonova, and M. N. Shchukina

We previously reported the synthesis and a study of the complex-forming properties of some alicyclic 1,2-diaminetetraacetic acids with a trans-configuration [1, 2]. In addition to this series, trans-1,2-diaminocyclohexene-(4)-N,N,N',N'-tetraacetic acid (I) was synthesized. The starting material for the preparation of this compound was the dimethyl ester of cis-cyclohexene-(4)-dicarboxylic-1,2 acid, which was prepared from the condensation product of butadiene and maleic anhydride. When the cis-diester was heated with hydrazine hydrate without solvent, the trans-dihydrazide was formed as in the case of the cyclohexane analog [1]. By means of the Curtius reaction, the trans-dihydrazide was converted into the dihydrochloride of the previously undescribed trans-1,2-diaminocyclohexene-(4), which was treated with excess chloroacetic acid in an alkaline medium to yield the tetraacid (I).

In order to study the effect of substituents on the complex-forming capacity of complexons of the ethylenediaminetetraacetic acid series, we synthesized 1-phenylethylenediamine-N,N,N',N'-tetraacetic acid (II). The 1,2-diaminoethylbenzene required for preparing this complexon was obtained by two methods: a) starting from acetophenone by nitrosation, oximination, and subsequent reduction of the dioxime with metallic sodium in alcohol in [3], and b) from β-phenyl-β-alanine by Rodionov's method [4].



(I)



(II)

We were unable to obtain the corresponding tetraacetic acid by condensation of the diamine with chloroacetic acid. It was synthesized by prolonged heating of 1,2-diaminoethylbenzene with excess bromoacetic acid in the presence of sodium hydroxide at 40°.

The complex-forming capacity of the compounds synthesized was evaluated by a chromatographic method [5]. Ethylenediaminetetraacetic acid (EDTA) was used for comparison. The cations Y^{3+}, Ca^{2+} and Sr^{2+}, containing the radioactive isotopes Y^{91}, Ca^{45} and Sr^{89}, respectively, were adsorbed on the cationite KU-2. The columns were eluted with a solution of complexon (concentration 0.003 M, pH 6.7) and the concentrations of elements in the eluate samples (~0.25 ml) were determined radiochemically. The amounts of eluted elements found in the samples were plotted on a graph of concentration of element in sample against volume of sample and from this we determined the volume of solution corresponding to the maximum content of element in the filtrate (V_{max}).

The table shows the results of chromatographic evaluation of the complex-forming capacity of the complexons synthesized in comparison with ethylenediaminetetraacetic acid and these indicate that both new complexons form complexes with Y, Ca, and Sr with a stability of the same order as with ethylenediaminetetraacetic acid.

Tetraacid \ Cations	Vmax (ml)		
	Y	Ca	Sr
I	4.2	7.4	12.7
II	4.2	7.3	12.5
EDTA	4.2	6.9	11.7

The data obtained on the relatively low complex-forming capacity of the dehydro analog (I) in comparison with trans-1,2-diaminocyclohexanetetraacetic acid confirm the hypotheses we put forward previously [2] on the factors affecting the stability of metal complexes formed by complexons of the EDTA series. Due to the double bond in it, the cyclohexene ring has a more rigid structure than the fully hydrogenated ring. Due to this, the possibility of the approach of two amino groups in a trans position is considerably reduced.

The results of studying the properties of complexon (II) show that the presence of a phenyl radical next to one of the amino groups in ethylenediaminetetraacetic acid has little effect on the complex-forming capacity.

EXPERIMENTAL

Dihydrazide of trans-cyclohexene-(4)-dicarboxylic-1,2 acid. 10 g of the diethyl ester of cis-cyclohexene-(4)-dicarboxylic-1,2 acid [6] was heated with 11 ml of 100% hydrazine hydrate at 130-140° for 20 hours. The mixture was treated with 100 ml of hot water and the white crystalline precipitate which formed on cooling was washed with water and alcohol. Recrystallization from 60% alcohol yielded 8.7 g of dihydrazide, which represents 51.5%, calculated on the diester; the m.p. was 202.5-203° (in a sealed capillary).

Found %: C 48.45, 48.50; H 7.32, H 6.99. $C_8H_{14}O_2N_4$. Calculated %: C 48.48; H 7.12.

Dihydrochloride of trans-1,2-diaminocyclohexene-(4). 7.42 g of the dihydrazide was dissolved in 26 ml of 10% hydrochloric acid, 70 ml of methylene chloride added, and a solution of 5.16 g of sodium nitrite in 12 ml of water introduced dropwise at 18-20°. The lower layer was separated and the aqueous one extracted with methylene chloride (2 × 30 ml). The combined methylene chloride solutions were dried with fused calcium chloride, filtered, and mixed with 40 ml of anhydrous alcohol. After removal of the methylene chloride by distillation (up to 78°), the solution was boiled for 2 hours, a solution of 30 g of potassium hydroxide in 90 ml of methyl alcohol added and the solution again boiled for 2 hours. The mixture was steam distilled and the distillate acidified with hydrochloric acid and evaporated to dryness. We obtained 3.4 g of the dihydrochloride, which had decomp. p. > 320° after recrystallization from 10% hydrochloric acid.

Found %: Cl 38.38, 38.52. $C_6H_{12}N_2 \cdot 2HCl$. Calculated %: Cl 38.11.

The dibenzoyl derivative of trans-1,2-diaminocyclohexene had m.p. 299.5-300.0° (from glacial acetic acid).

Found %: C 74.87; H 6.23. $C_{20}H_{20}O_2N_2$. Calculated %: C 74.98; H 6.29.

Trans-1,2-diaminocyclohexene-N,N,N',N'-tetraacetic acid. 5 g of the dihydrochloride of trans-1,2-diaminocyclohexene was treated with 12.7 g of monochloroacetic acid and 47 ml of 7 N sodium hydroxide solution at 95° for 3.5 hours. Acidification to pH 1.5 with hydrochloric acid yielded 11.4 g of the tetraacid (58%) with m.p. 190-192° (from water). After being dried over phosphorus pentoxide, the acid contained 1 molecule of water of crystallization.

Found %: C 46.37; H 6.19; N 7.82. $C_{14}H_{20}O_8N_2 \cdot H_2O$. Calculated %: C 46.40; H 6.11; N 7.73.

1,2-Diaminoethylbenzene was obtained by the Hofmann reaction from the amide of β-phenyl-β-alanine [4] and also by reduction of phenylglyoxime with sodium in alcohol [3]. The second method was found to be more convenient; from 5 g of glyoxime we obtained 4.5 g of the dihydrochloride of 1,2-diaminoethylbenzene (71%) with m.p. 300-301° (from conc. HCl) (decomp.).

Found %: Cl 33.79. $C_8H_{12}N_2 \cdot 2HCl$. Calculated %: Cl 33.91.

The dibenzoyl derivative had m.p. 223.5° (from alcohol).

Found %: C 76.88; H 6.00; N 8.00. $C_{22}H_{20}O_2N_2$. Calculated %: C 76.72; H 5.85; N 8.13.

1-Phenylethylenediaminetetraacetic acid. Over a period of 8 hours, 7 N sodium hydroxide solution was added to a mixture of 2 g of the dihydrochloride of 1-phenylethylenediamine and 6.65 g of bromoacetic acid at 40-50° to keep the pH of the medium at 10-11. The cooled solution was neutralized to pH 6-7, decolorized by boiling with charcoal and acidified to pH 1-2 with hydrochloric acid. We obtained 2.2 g of crude tetraacid. After recrystallization from water, the product had m.p. 127.5-150°(decomp.).

Found %: C 49.72; H 5.78; N 6.97. $C_{16}H_{20}O_8N_2 \cdot H_2O$. Calculated %: C 49.74; H 5.71; N 7.24.

SUMMARY

1. The previously undescribed trans-1,2-diaminocyclohexene-(4)- and 1-phenylethylenediaminetetraacetic acids were synthesized.

2. By means of a chromatographic method it was shown that both new complexons have a complex-forming capacity of the same order as ethylenediaminetetraacetic acid.

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AROMATIC PROPERTIES OF SYDNONES

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Among the so-called mesoionic compounds, the sydnones are of especial interest. From 1935, when the first representative, 3-phenylsydnone, was synthesized [1], up to the present time, the study of the synthesis and properties of these peculiar heterocycles has continued. Being extremely reactive compounds, sydnones readily undergo a whole series of conversions. One of the interesting properties of sydnones is the substitution capacity of the hydrogen atom in position four. Thus, when 3-phenylsydnone was treated with a mixture of nitric and sulfuric acids at −10°, 4-nitro-3-phenylsydnone was isolated [2]. The hydrogen atom in position four replaced by bromine and chlorine with exceptional ease [2, 3].

(A)

On the basis of these data a hypothesis was put forward on the aromatic character of sydnones, which was confirmed by an examination of the electronic structure of these heterocycles [4]. In the five-membered ring of a sydnone, there are only 7π electrons in the 2pZ state; one of these may be donated to the exocyclic oxygen atom and as a result of this some negative charge is concentrated on it, while 6π electrons remain in the ring, which has a certain positive charge, and form the aromatic system. On the basis of these arguments, the formula given was put forward to represent sydnones.

At the present time there are insufficient experimental data confirming the aromatic properties of sydnones, which are unsubstituted in position four; therefore, investigations in this direction are of undoubted interest.

We sulfonated a series of sydnones with dioxane−sulfur trioxide in dichloroethane solution at 20-40°. The reaction was carried out with 3-phenyl-, 3-(p-methoxyphenyl)-, 3-(p-ethoxyphenyl)-, 3-(m-chlorophenyl)- and 3-ethylsydnones. We prepared the last three compounds for the first time. They were obtained by treating appropriate N-nitroso-α-amino acids with acetic anhydride.

After sulfonation, the reaction mixture was processed in the usual way; the sulfonic acids were isolated as the barium salts, from which the benzylthiuronium derivatives of the acids were prepared. Treatment of the barium salt of 3-phenylsydnone-4-sulfonic acid with sodium sulfate gave its sodium salt. The free acid could not be isolated by neutralization of the barium salt with sulfuric acid, since this treatment caused cleavage of the sulfonic acid group and 3-phenylsydnone was formed.

As the second reaction characteristic of aromatic compounds, we chose mercuration.

When an aqueous alcohol solution of 3-phenylsydnone was treated with mercuric chloride, two compounds were isolated: 4-chloro-(3-phenylsydnone)-mercury and di-4-(3-phenylsydnone)-mercury. The reaction with 3-p-ethoxyphenylsydnone proceeded similarly, but the chloromercury derivative could not be finally freed from traces of the symmetrical compound. The mercuration of 3-phenylsydnone with mercuric acetate gave a good yield of 4-acetatomercuri-3-phenylsydnone. Treatment of this with a solution of sodium chloride led to the

formation of the chloromercurisydnone and the symmetrical derivative, which was obtained in the greatest amount.*

The ease of replacement of the hydrogen atom in sydnones by a sulfonic acid group and mercury thus confirmed that these compounds had aromatic properties.

Although the infrared spectra of some sydnones have already been described in the literature [6], it was interesting to obtain similar data for the compounds we synthesized for the first time, 3-ethyl-, 3-(m-chlorophenyl)- and 3-(p-ethoxyphenyl)-sydnones and also for the salts of m-chlorophenylsydnone-4-sulfonic acid. As in the previously published spectra of 3-phenylsydnone (and some other sydnones), attention was attracted by the presence of a sharp and very intense absorption band corresponding to a carbonyl group. The position of this band (1740-1770 cm^{-1}) characterized this carbonyl group as being comparatively little polarized and similar to the carbonyl in γ-lactones.

In connection with this fact, it should be noted that the representation of the structure of sydnones by Formula (A), which is most widely accepted at the present time, cannot be considered satisfactory, since it does not reflect the comparatively high multiplicity of the C=O bond, which considerably exceeds, for example, the corresponding multiplicity in amides, aromatic ketones, and other similar compounds, for which, however, this bond is represented in the form of C=O and not C−$\overline{O}$.

In the region of C−H oscillation frequencies, the spectrum of 3-ethylsydnone showed two comparatively low-intensity bands at 2978 and 3097 cm^{-1}. The first band pertains to oscillations of the C−H groups in the ethyl radical; the second band occupies a position corresponding to C−H bonds in aromatic or ethylene compounds. Undoubtedly this band is connected with oscillations of the C−H bond at position 4 and the high value of the frequency (3097 cm^{-1}) may be considered as a confirmation of the aromatic character of sydnones. Evidently, this band is also present in the spectra of 3-arylsydnones, but in these cases it is overlaid by absorption caused by oscillations of C−H bonds of the phenyl ring (3100 cm^{-1}).

Among the other bands in the spectra of sydnones, one notices the quite intense band in the region of 950-960 cm^{-1}, which was systematically observed for all the compounds and possibly it pertained to a symmetrical oscillation of the five-membered ring of sydnones (with the benzene series, this oscillation appears as a band in the region of 980-1000 cm^{-1}).

This band is evidently strongly displaced or disappears completely from the spectrum of the barium salt of m-chlorophenylsydnone-4-sulfonic acid, in which the intense band of the carbonyl group is retained; bands of average intensity at 3400-3450 cm^{-1} were caused by water of crystallization in the substance.

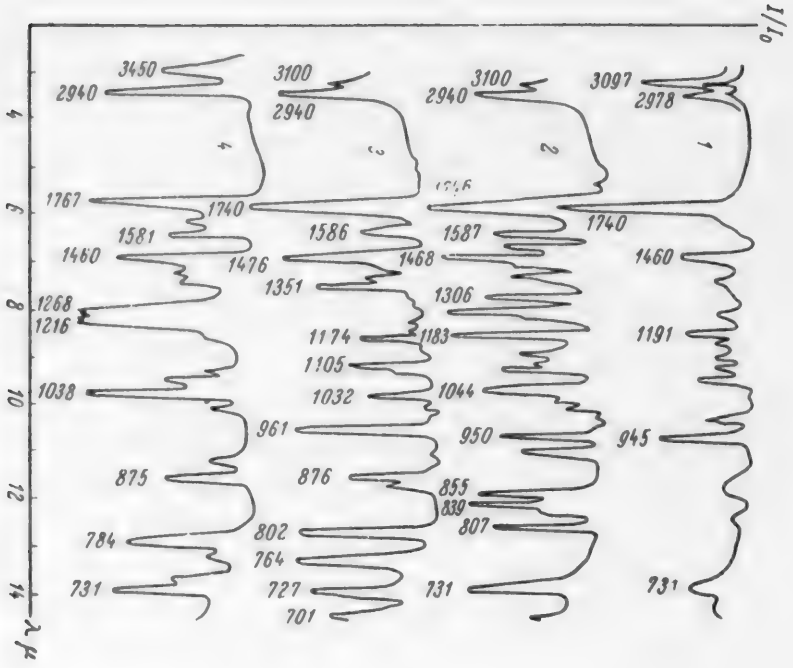
EXPERIMENTAL

N-p-ethoxyphenylglycine. A mixture of 75 ml of p-phenetedine, 28.4 g of chloroacetic acid and 120 ml of water was heated for 1.5 hours on a boiling water bath with the reaction flask shaken from time to time. The reaction mass was poured into a porcelain mortar, powdered when cool and washed with water to remove phentidine hydrochloride. The residue was recrystallized from water to yield 40 g of N-p-ethoxyphenylglycine with m.p. 159-162° (decomp.).

N-Nitroso-N-(p-ethoxyphenyl)-glycine. To a solution of 35 g of N-(p-ethoxyphenyl)-glycine in 450 ml of 15% hydrochloric acid at 0° was slowly added a solution of 12.2 g of sodium nitrite in 35 ml of water. After 1.5 hours stirring at 0°, the yellow precipitate of the nitroso compound was collected and washed first with 10% hydrochloric acid and then with water. The yield was 32 g and the m.p. 91-92° (decomp.).

3-(p-Ethoxyphenyl)-sydnone. 32 g of N-nitroso-N-(p-ethoxyphenyl)-glycine was mixed with a five-fold amount of acetic anhydride and left to stand at room temperature in the dark. The reaction product partly precipitated. After two days, the mixture was poured into 900 ml of water. The mixture was neutralized with sodium bicarbonate and the precipitate of 3-p-ethoxyphenylsydnone collected and washed with water. The yield was 28 g. After recrystallization from alcohol, the product had m.p. 127-128° (decomp.).

* When the present work had been carried out, an abstract appeared on the work of Japanese chemists [5], in which a short report was given on the mercuration of sydnones. Our results agree completely with those described.



Infrared absorption spectra: 1) 3-ethylsydnone (liquid, 0.01 mm layer); 2) 3-(p-ethoxyphenyl)-sydnone; 3) 3-(m-chlorophenyl)-sydnone; 4) barium salt of 3-(m-chlorophenyl)-sydnone-4-sulfonic acid (all in the crystalline state, suspensions in vaseline oil).

Found %: C 58.03; H 4.90. $C_{10}H_{10}O_3N_2$. Calculated %: C 58.24; H 4.88.

N-(m-Chlorophenyl)-glycine. 32 g of m-chloroaniline, 41.5 g of ethyl bromoacetate, 30 g of sodium acetate and 25 ml of anhydrous alcohol were heated for 5 hours at 125°. Then 100 ml of water was added. The precipitate was collected and washed with water to yield 33.5 g of ester.

33.5 g of the ethyl ester of N-(m-chlorophenyl)-glycine was boiled with a solution of 9.5 g of NaOH in 128 ml of water and 13 ml of alcohol for 30 minutes. The filtered solution was acidified with concentrated hydrochloric acid. The precipitate was collected and dried in a vacuum desiccator over alkali to yield 25 g of N-(m-chlorophenyl)-glycine with m.p. 96.5-97.5° (decomp.).

N-Nitroso-N-(m-chlorophenyl)-glycine. To a suspension of 25 g of N-(m-chlorophenyl)-glycine in 250 ml of water at 0° was slowly added a solution of 10 g of sodium nitrite in 38 ml of water. After complete solution, stirring was continued for a further 2 hours and then 15.8 ml of hydrochloric acid (d 1.19) added, and the precipitate collected and dried in a vacuum desiccator over alkali. We obtained 26.8 g of the nitroso compound with m.p. 106.5-107.5° (decomp.).

3-(m-Chlorophenyl)-sydnone. 26.8 g of N-nitroso-N-(m-chlorophenyl)-sydnone was heated on a boiling water bath with a five-fold amount of acetic anhydride for 1.5 hours. The acetic anhydride was removed in vacuum. The residue was recrystallized from alcohol to give 18.2 g of 3-(m-chlorophenyl)-sydnone with m.p. 144.5-145.5° (decomp.).

Found %: C 48.91; H 2.62; Cl 18.16. $C_8H_5O_2N_2Cl$. Calculated %: C 48.87; H 2.56; Cl 18.03.

N-ethylglycine. To a solution of 14 g of ethylamine in 150 ml of benzene was added a solution of 17 ml of ethyl bromoacetate. The mixture was heated for 2 hours and after cooling, the precipitate was collected. The filtrate and benzene wash solution were treated with 60 ml of 3.0 N H_2SO_4 and the aqueous layer separated and boiled with 750 ml of 0.5 N $Ba(OH)_2$ solution in a stream of nitrogen for 2.5 hours. The solution obtained was acidified with the calculated amount of H_2SO_4 to remove the barium ions, filtered, and evaporated to dryness in vacuum. We obtained 10.2 g of N-ethylglycine with m.p. 175-177° (decomp.).

3-Ethylsydnone. To a solution of 10 g of N-ethylglycine in 50 ml of water and 9.7 ml of concentrated hydrochloric acid, cooled to 0°, was slowly added a solution of 8.3 g of sodium nitrite in 20 ml of water. After 3 hours stirring, the nitroso compound was extracted with ether. The ether solution was dried with baked sodium sulfate and to it was added 65 ml of acetic anhydride. The ether was removed by distillation and the reaction mass heated on a water bath for 3 hours and then left at room temperature for a day. The acetic anhydride was removed at reduced pressure, and vacuum distillation of the residue yielded 5.3 g of 3-ethylsydnone as a light yellow, mobile liquid with b.p. 137.5-138° at 0.6 mm.

Found %: C 41.82; H 5.51; N 24.20. $C_4H_6O_2N_2$. Calculated %: C 42.10; H 5.30; N 24.55.

Sulfonation of 3-phenylsydnone. With strong cooling, 12.1 ml of anhydrous dioxane was added slowly to a solution of 11.3 g of sulfur trioxide in 90 ml of dry dichloroethane. With cooling, a solution of 9 g of 3-phenylsydnone with m.p. 134-135° [1] in dry dichloroethane was gradually added to the suspension of dioxane–sulfur trioxide obtained and the mass stirred for 1 hour at 0°. The reaction mixture was left at room temperature for a day. The clear solution was treated with an aqueous suspension of barium carbonate and then the dichloroethane and dioxane were evaporated on a water bath. The reaction mass was filtered in the hot state. Unreacted 3-phenylsydnone (2.5 g) was isolated from the cold filtrate. The solution of barium salts was evaporated to dryness and the residue recrystallized from a small amount of water and dried in a vacuum desiccator over phosphorus pentoxide. We obtained 11.2 g of the barium salt of 3-phenylsydnone-4-sulfonic acid (90%, calculated on the 3-phenylsydnone reacting). The barium salt decomposed at 85°.

Found %: Ba 21.05. $C_8H_5O_5N_2SBa_{1/2} \cdot H_2O$. Calculated %: Ba 20.94.

To an aqueous solution of the barium salt was added an aqueous solution of S-benzylthiuronium chloride. On cooling, crystals of the benzylthiuronium salt of 3-phenylsydnone-4-sulfonic acid precipitated and these were recrystallized from aqueous alcohol. The m.p. was 167-168° (decomp.).

Found %: C 47.18; H 4.04; S 15.62. $C_8H_6O_5N_2S \cdot C_8H_{10}N_2S$. Calculated %: C 47.06; H 3.94; S 15.70.

9 g of 3-(m-chlorophenyl)-sydnone was sulfonated with dioxane–sulfur trioxide as described above. The ratio of sulfonating agent to sydnone was 3:1. After stirring the reaction mixture (1 hour at 0° and 2 hours at room temperature), we isolated 4 g of the barium salt of 3-(m-chlorophenyl)-sydnone-4-sulfonic acid, which was recrystallized from water and dried in a vacuum desiccator over phosphorus pentoxide. The salt decomposed at 93°.

Found %: Ba 19.20. $C_8H_4O_5N_2ClSBa_{1/2} \cdot H_2O$. Calculated %: Ba 18.95.

The benzylthiuronium salt of 3-(m-chlorophenyl)-sydnone-4-sulfonic acid had decomp. p. 161-162° (from dilute alcohol).

Found %: C 43.57; H 3.39; S 14.22. $C_8H_5O_5N_2ClS \cdot C_8H_{10}N_2S$. Calculated %: C 43.39; H 3.41; S 14.47.

0.766 g of the barium salt of 3-(m-chlorophenyl)sydnone-4-sulfonic acid was dissolved in water and a solution of 0.150 g of anhydrous sodium sulfate added. The barium sulfate precipitate was collected and the filtrate tested for the complete precipitation of barium and the absence of excess Na_2SO_4. The filtrate was treated with activated charcoal and evaporated to dryness. The sodium salt of 3-(m-chlorophenyl)-sydnone-4-sulfonic acid formed a white, crystalline powder, decomposing at 115-120°.

4 g of 3-(p-ethoxyphenyl)-sydnone was sulfonated by the method described above. The ratio of sulfonating agent to sydnone was 3:1. The mixture was stirred for 3 hours at room temperature and heated for 1 hour at 40° and then we isolated 1.5 g of the barium salt of 3-(p-ethoxyphenyl)-sydnone-4-sulfonic acid, which was recrystallized from water and dried in a vacuum desiccator over phosphorus pentoxide. The substance decomposed at 93°.

Found %: Ba 17.62. $C_{10}H_9O_6N_2SBa_{1/2} \cdot 2H_2O$. Calculated %: Ba 17.61.

The benzylthiuronium salt of 3-(p-ethoxyphenyl)-sydnone-4-sulfonic acid had decomp. p. 132-134° (from water).

Found %: C 47.87; H 4.64; S 14.13. $C_{10}H_{10}O_6N_2S \cdot C_9H_{10}N_2S$. Calculated %: C 47.77; H 4.45; S 14.17.

3-(p-Methoxyphenyl)-sydnone (m.p. 125-126°) [7] was sulfonated similarly to 3-phenylsydnone.

The benzylthiuronium salt of 3-(p-methoxyphenyl)-sydnone-4-sulfonic acid had decomp. p. 131.5-133° (from dilute alcohol).

Found %: C 46.69; H 4.30; S 14.51. $C_9H_8O_6N_2S \cdot C_9H_{10}N_2S$. Calculated %: C 46.56; H 4.13; S 14.62.

3.2 g of 3-ethylsydnone was treated with sulfur trioxide–dioxane complex similarly to yield 6.1 g of the barium salt of 3-ethylsydnone-4-sulfonic acid. The benzylthiuronium salt had decomp. p. 137-138° (from water).

Found %: C 39.93; H 4.54; S 17.74. $C_4H_6O_6N_2S \cdot C_9H_{10}N_2S$. Calculated %: C 39.98; H 4.46; S 17.78.

Mercuration of 3-phenylsydnone. A mixture of 3.6 g of 3-phenylsydnone, 6 g of mercuric chloride and 7.26 g of sodium acetate in 150 ml of 50% methanol was boiled on a water bath for 5 hours. After a few minutes, complete solution occurred and then a precipitate appeared. It was collected from the hot solution and washed with acetone and hot water. We obtained 3.7 g of di-(3-phenylsydnone)-mercury with m.p. 274.5-275°.

Found %: N 10.78; Hg 38.40. $C_{16}H_{10}O_4N_4Hg$. Calculated %: N 10.71; Hg 38.36.

Cooling the aqueous alcohol mother solution yielded 2.1 g of a substance with m.p. 193-195° (from acetone). The substance contained chlorine (Beilstein test) and the amount of nitrogen found in it corresponded to 4-chloro-(3-phenylsydnone)-mercury.

Found %: N 7.11. $C_8H_5O_2N_2ClHg$. Calculated %: N 7.05.

To a solution of 2.69 g of mercuric acetate in 15 ml of water was added a solution of 1.5 g of 3-phenylsydnone in 30 ml of acetone. After a few minutes, a white precipitate of 4-acetatomercuri-3-phenylsydnone formed. The weight was 3.3 g and the m.p. 203.5-204.5° (from acetone).

Found %: N 6.64; Hg 46.90. $C_{10}H_8O_4N_2Hg$. Calculated %: N 6.65; Hg 47.67.

Dissolving 4-acetatomercuri-3-phenylsydnone in a large amount of water and adding to the boiling solution an equimolar amount of sodium chloride yielded a precipitate, which consisted of a mixture of two substances: mainly di-(3-phenylsydnone)-mercury and a small amount of 4-chloro-(3-phenylsydnone)-mercury.

Mercuration of 3-(p-ethoxyphenyl)-sydnone. 2.5 g of 3-(p-ethoxyphenyl)-sydnone, 3.29 g of mercuric chloride, 3.98 g of sodium acetate and 90 ml of 50% methyl alcohol were boiled on a water bath for 5 hours. The hot reaction mass was filtered to yield 2.28 g of di-(p-ethoxyphenylsydnone)-mercury with m.p. 222.5 – 223.5° (from alcohol).

Found %: N 9.15; Hg 32.60. $C_{20}H_{18}O_6N_4Hg$. Calculated %: N 9.17; Hg 32.83.

Cooling the aqueous alcohol mother solution yielded 1.32 g of a substance which was a mixture of di-(p-ethoxyphenylsydnone)-mercury and 4-chloro-(3-p-ethoxyphenylsydnone)-mercury. We were unable to obtain 4-chloro-(3-p-ethoxyphenylsydnone)-mercury in a pure state due to the small difference between its solubility and that of di-(p-ethoxyphenylsydnone)-mercury.

SUMMARY

1. 3-(p-Ethoxyphenyl)-sydnone, 3-(m-chlorophenyl)-sydnone and 3-ethylsydnone were synthesized for the first time.

2. It was found that sydnones readily undergo sulfonation and mercuration, which are characteristic reactions of aromatic compounds.

3. Data obtained by studying the IR spectra of sydnones confirm the aromatic character of these compounds. The presence of bands corresponding to a carbonyl group in the spectra is not in accord with the formula for the structure of sydnones accepted at the present time.

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DIENE SYNTHESIS OF ALLOOCIMENE WITH UNSYMMETRICAL DIENOPHILES

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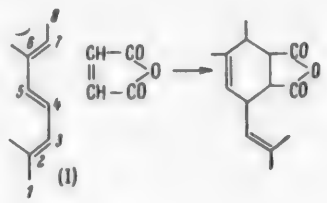
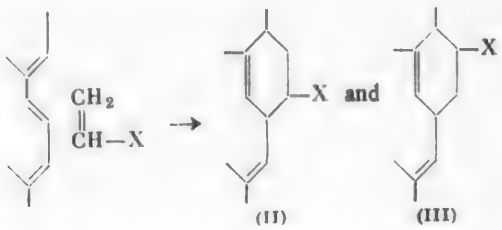
The diene synthesis of alloocimene (I) may be achieved through the different pairs of conjugated bonds in positions 2,5 and 4,7.

It was recently proved rigidly by us [1] and later, almost simultaneously, by other investigators [2, 3] that the diene synthesis of alloocimene with maleic anhydride proceeds at carbon atoms 4 and 7.



(I)

In the case of unsymmetrical dienophites, addition at carbon atoms 4 and 7 of alloocimene may give two isomeric products, (II) and (III).

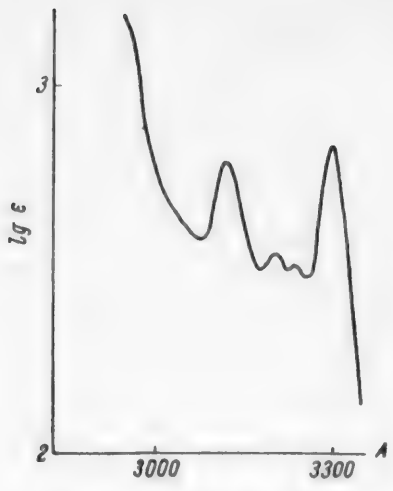


(II) (III)

There are no definite indications in the literature on whether the diene synthesis proceeds to form products with structure (II) or (III) or a mixture of the two isomers.

Chrétien-Bessière [2] carried out the diene synthesis reaction of alloocimene with acrylamide ($X = CONH_2$). On the basis of paper [4], where it was shown that in the case of 2-phenylbutadiene and acrylamide, diene synthesis loses its stereospecificity, Chrétien-Bessière considered that a mixture of the two products (II) and (III) was obtained. However, he did not separate and isolate these products.

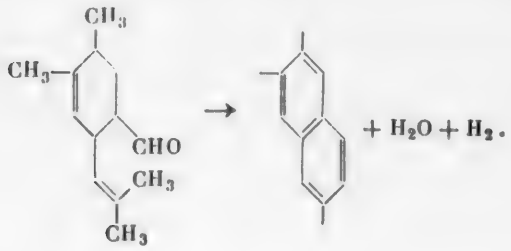
In order to determine the structure of the diene synthesis products of alloocimene with unsymmetrical dienophiles and decide between structures (II) and (III), we carried out the diene synthesis of alloocimene with acrolein, methyl acrylate and acrylonitrile and determined the structures of the products. The product from diene synthesis with alloocimene and acrolein has been obtained previously [5]. It structure was demonstrated



Ultraviolet absorption spectra of 2,3,6-trimethylnaphthalene (spectrum for the range 3000-3300 A).

by dehydrogenation over palladized charcoal. The dehydrogenation gave a high yield of a crystalline product with m.p. 100-101°, which was shown by its melting point and that of its picrate (m.p. 129-130°) [6] and also by the ultraviolet absorption spectrum [7] (see figure) to be 2,3,6-trimethylnaphthalene.

The formation of 2,3,6-trimethylnaphthalene demonstrates the structure of the adduct of alloocimene with acrolein (II, X = CHO).

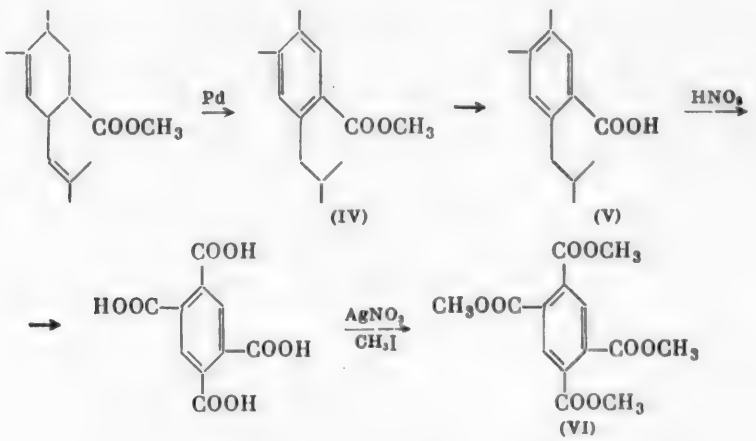


The dehydrogenation of adduct (II) is a convenient method of synthesizing 2,3,6-trimethylnaphthalene.

In the same paper [2], a description was given of the preparation of 2,3,6-trimethylnaphthalene from the adduct of alloocimene with maleic anhydride by heating it with phosphorus pentoxide [8]. In this case, the yield of the pure product was extremely low (9.4%).

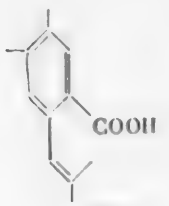
By the interaction of alloocimene with methyl acrylate, we obtained an adduct in 81.5% yield on the alloocimene reacting.

Hydrolysis of the ester yielded the free acid with m.p. 85-87°. That the ester had structure (II) (X = $COOCH_3$) was demonstrated in the following way. Dehydrogenation of the adduct over palladized charcoal yielded the ester (IV).



Hydrogenation of a double bond in a side chain during a dehydrogenation reaction was observed in dehydrogenation of the adduct from alloocimene and maleic anhydride [2] and also in the case of p-menthadiene-1,8,9-carboxylic-7 acid [9]. Hydrolysis yielded the free acid with m.p. 127-129.5° (V). Oxidation of the acid with nitric acid gave pyromellitic acid, which was identified as its tetramethyl ester (VI) with m.p. 141-142° [10]. If the dehydrogenation of the adduct of alloocimene with methyl acrylate over palladized charcoal were accompanied by reduction of the double bond in the side chain and formation of ester (V), then reduction of the double bond should not occur if sulfur were used as the dehydrogenating agent.

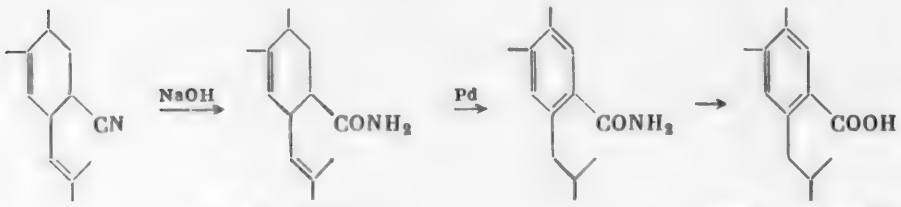
We dehydrogenated the adduct of alloocimene with methyl acrylate by means of sulfur in the presence of sodium sulfide to increase the yield of dehydrogenation product [11] and obtained acid (VII) with m.p. 117-118°. Its structure was demonstrated by oxidation with nitric acid to pyromellitic acid (the tetramethyl ester had m.p. 141-142°). When the product of diene synthesis with alloocimene and maleic anhydride was dehydrogenated with sulfur previously [2], the reaction proceeded similarly.



(VII)

Acrylonitrile smoothly underwent diene synthesis with alloocimene to give an adduct in 77.9% yield, calculated on the alloocimene reacting. That its structure was similar to (II) (X = CN) was demonstrated in the following way. Hydrolysis of the nitrile in an alkaline medium led to amide (VIII) with m.p. 141-142°.* We were unable to hydrolyze the amide directly to the acid.

Dehydrogenation of the amide with m.p. 141-142° over palladized charcoal yielded amide (IX), which melted at 152° without further purification. Its hydrolysis by Bouveault's method [12] led to an acid with m.p. 126-128°, undepressed by admixture with (V). The reactions described may be illustrated by the following scheme:



m.p. 141–142° (VIII)

(IX)

m.p. 126–128°

Thus, in the cases we considered of diene synthesis with alloocimene and acrolein, methyl acrylate and acrylonitrile, the dienophile was added to form adduct (II). We cannot exclude the possible formation of small amounts of adducts (III), but they were not detected in the present investigation.

EXPERIMENTAL

Preparation of adduct of alloocimene with acrolein. The adduct was obtained under the conditions described by B. A. Arbuzov [5]. 143.6 g of alloocimene, 64.6 g of acrolein, and 0.3 g of hydroquinone were heated in a sealed tube for 2 hours at 115-118°; distillation of the reaction product on a column of 27 theoretical plates yielded 111.6 g of adduct as a mobile, oily liquid with a pleasant grass-like smell (the yield was 77.8% calculated on the alloocimene reacting).

B.p. 122-124° (6.5 mm), $n^{20}D$ 1.4925, d^{20}_4 0.9306, MR_D 60.04. $C_{13}H_{20}O$. Calculated 59.11.

Dehydrogenation of adduct of alloocimene and acrolein over palladized charcoal. Heating 3.9 g of adduct with 0.85 g of palladium on charcoal [13] on a Wood's bath at 220-240° for 3 hours yielded 3.3 g of a paraffin-like mass and three recrystallizations of this from methyl alcohol gave a crystalline product in the form of very fine, lustrous platelets with m.p. 100-101°, corresponding to 2,3,6-trimethylnaphthalene.

The picrate had m.p. 129-130° [6].

Found %: C 91.50, 91.60; H 8.40, 8.30. $C_{13}H_{14}$. Calculated %: C 91.71; H 8.29.

Preparation of adduct of alloocimene with methyl acrylate. Heating 143.7 g of alloocimene with excess methyl acrylate in a sealed tube at 130-140° for 3 hours and distillation of the reaction products on a column of 27 theoretical plates yielded 60.3 g of adduct (81.5% yield, calculated on the alloocimene reacting) in the form of a mobile, oily liquid with a very weak, pleasant smell.

*The addition of acrylamide to alloocimene [2] yielded an amide with m.p. 139-140°, which was taken as a mixture of (II) and (III) ($X = CONH_2$). The reaction product was not resolved. Hydrolysis of the amide with HBr yielded an acid with m.p. 130-131°, which was also taken as a mixture of isomers.

B.p. 105° (2.5 mm), $n^{20}D$ 1.4824, d^{20}_4 0.9597. MR_D 66.08. $C_{14}H_{22}O_2F_2$. Calculated 65.37.

Found %: C 75.05, 75.25; H 9.97, 9.95. $C_{14}H_{22}O_2$. Calculated %: C 75.63; H 9.97.

Hydrolysis of adduct of alloocimene and methyl acrylate with alkali in aqueous alcohol. 8 g of adduct with b.p. 105° (2.5 mm) and 4 g of NaOH in 8 ml of water and 40 ml of alcohol were heated for 5 hours. Removal of the alcohol and acidification of the reaction mixture with dilute sulfuric acid yielded the hydrolysis product as a yellow oil (7.7 g), which crystallized when ligroine was added. Four recrystallizations from aqueous alcohol yielded an acid with m.p. 85-87°; on slow crystallization, the product formed long, coarse platelets.

Found %: C 75.08, 75.11; H 9.67, 9.75. $C_{13}H_{20}O_2$. Calculated %: C 74.94; H 9.68.

Dehydrogenation of adduct of alloocimene with methyl acrylate over palladized charcoal. 20.8 g of adduct with b.p. 105° (2.5 mm) and 10 g of palladized charcoal were heated for 6 hours at 230-250°. Distillation of the reaction product from an Arbuzov flask yielded a fraction (9 g) as a quite thick, odorless liquid, which was investigated.

B.p. 127-129° (4 mm), n^{20}_DS 1.5055, d^{20}_4 0.9883, MR_D 66.17. $C_{14}H_{20}O_2F_2$. Calculated 64.90.

Hydrolysis of hydrogenation product from adduct of alloocimene and methyl acrylate with alkali in aqueous alcohol. 2 g of dehydrogenated adduct (IV) with b.p. 127-129° (4 mm) and 1 g of NaOH in 10 ml of water and 15 ml of alcohol were heated for 7 hours. Removal of the alcohol and acidification with dilute hydrochloric acid yielded acid (V), which was recrystallized from ligroine; the m.p. was 127-129.5°.

Found %: C 75.90, 75.80; H 8.89, 8.80. $C_{13}H_{18}O_2$. Calculated %: C 75.69; H 8.79.

The silver salt was obtained from acid (V) through the ammonium salt by the usual method and analyzed.

Found %: Ag 34.47, 34.39. $C_{13}H_{17}O_2Ag$. Calculated %: Ag 34.45.

Oxidation of hydrolyzed and dehydrogenated adduct (V) with dilute nitric acid. 0.7 g of acid (V) with m.p. 127-129.5° and 10 ml of NHO_3 (d 1.1) were heated for 2.5 hours in a sealed tube at 200°. The acid dissolved. After removal of the nitric acid and evaporation, the residue (0.8 g) was washed with alcohol and ether and converted into the silver salt (1.15 g) by the usual method; methylation of the latter with methyl iodide yielded ester (VI) with m.p. 141.5-142° (from methyl alcohol) [10].

Found %: C 54.29, 54.36; H 4.60, 4.57. $C_{14}H_{14}O_6$. Calculated %: C 54.19; H 4.55.

Preparation of adduct of alloocimene with acrylonitrile. By the method described above, from 140.6 g of alloocimene, 60.7 g of acrylonitrile and 0.3 g of hydroquinone we obtained 72.7 g of adduct with a pleasant, flower-like smell (77.9% yield, calculated on the alloocimene reacting).

B.p. 125-129° (6.5 mm), $n^{20}D$ 1.4906, d^{20}_4 0.9180, MR_D 59.67. $C_{13}H_{19}NF_2$. Calculated 58.87.

Found %: C 82.50, 82.60; H 10.11, 10.20. $C_{13}H_{19}N$. Calculated %: C 82.48; H 10.10.

Hydrolysis of adduct of alloocimene and acrylonitrile with alkali in aqueous alcohol. 11.5 g of adduct with b.p. 125-129° (6.5 mm) and 5.1 g of NaOH in 8 ml of H_2O and 50 ml of alcohol were heated under reflux for 20 hours. After removal of the alcohol, the residue yielded a solid hydrolysis product (VIII) (5 g), which was readily soluble in ether, alcohol and acetone and difficultly so in ligroine. After four recrystallizations from aqueous methanol, the product melted at 141-142° [2]. On slow crystallization, the product formed very fine filaments, joined together in brushes.

Found %: C 74.92, 74.87; H 10.21, 10.26. $C_{13}H_{21}ON$. Calculated %: C 75.32; H 10.21.

Dehydrogenation of amide (VIII) over palladized charcoal and Bouveault hydrolysis of the aromatic amide (IX) obtained. 5 g of amide with m.p. 141-142° and 2.5 g of palladized charcoal were heated for 2.5 hours at 210-240°. Ether extraction in the cold yielded product (IX) with m.p. 152°. It was not purified further.*

0.6 g of amide (IX) was hydrolyzed by Bouveault's method [12]. We isolated 0.25 g of an acid with m.p. 126-128°. A mixed melting point with acid (V) was not depressed.

* M.p. 162-164° is given for the dehydrogenation product of the adduct of acrylamide and alloocimene [2].

SUMMARY

Diene synthesis was carried out with alloocimene and methyl acrylate and acrylonitrile. The structures of the adducts of alloocimene with acrolein, methyl acrylate, and acrylonitrile were determined.

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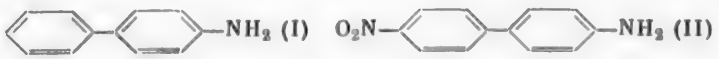
STERIC STRUCTURE AND REACTIVITY

XIV. INTERACTION OF ATOMIC GROUPINGS SEPARATED BY ONE, TWO, AND THREE BENZENE NUCLEI FROM THE DATA OF KINETIC INVESTIGATIONS OF THE REACTIONS OF AROMATIC AMINES WITH PICRYL CHLORIDE

L. M. Litvinenko, N. F. Levchenko, B. M. Krasovitskii, and N. I. Titarenko

Khar'kov State University

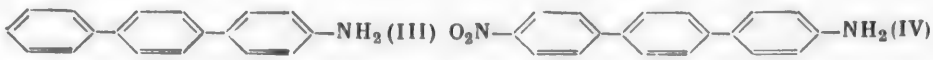
As a result of investigations of the kinetics of the acylation of 4-aminobiphenyl (I) and 4-amino-4'-nitrobiphenyl (II), on the one hand, and aniline and p-nitroaniline, on the other, in our laboratory it was recently established that the effect of a nitro group on the reactivity of an aromatic amino group was hundreds of times weaker in the biphenyl molecular system than in the benzene system [1]. The ratio of the rate constants for reactions of the amino and aminonitro derivatives, for example, K_I/K_{II} (f factor), can serve as a measure of the



quantitative value of this effect [2-5].

By using the same kinetic method, in the present work we wished to determine how an NO_2 group would affect the reactivity of an NH_2 group when these groups were separated by a system of three benzene nuclei. As a model reaction for this purpose, we chose the reaction of aromatic amines with picryl chloride in benzene solution, which has been found to be very sensitive to structural changes in the amine molecule [6] and hence may be used successfully for a quantitative characterization of the effect of the smallest differences in structure of these substances on the reactivity of the aromatic amino group.

In accordance with the above, we investigated the kinetics of the reaction of 4-amino-p-terphenyl (III) and 4-amino-4"-nitro-p-terphenyl (IV) with picryl chloride in benzene and the results obtained were compared with



kinetic data for the reactions of picryl chloride with aniline, 4-aminobiphenyl and 4-amino-4'-nitrobiphenyl, which were presented in a previous article [7]. To be able to compare the molecular systems of benzene, biphenyl, and p-terphenyl with respect to their efficiency in transferring the electronic effects of the para-substituents mentioned above, we augmented the experimental material previously available to us [7] with an investigation of the kinetics of the reaction of p-nitroaniline with picryl chloride.

EXPERIMENTAL

I. Preparation and Purification of Starting Materials

Benzene and picryl chloride were purified as described previously [7].

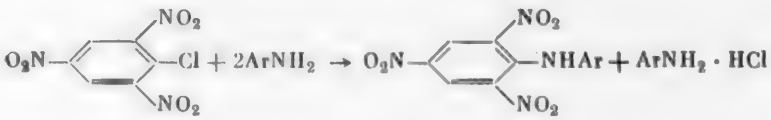
4-Amino-p-terphenyl was obtained by the procedure of [8] and further purified in the following way. The amine hydrochloride was precipitated from a benzene solution by the passage of dry hydrogen chloride. The amine isolated from this salt by treatment with aqueous ammonia was again subjected to this operation and the free base was then recrystallized twice from alcohol with activated charcoal and 3 times with benzene. After drying in vacuum at 100°, the amine had m.p. 198°.

4-Amino-4"-nitro-p-terphenyl was also prepared by the method we proposed [8] and further purified. The amine was precipitated from nitrobenzene as the hydrochloride with dry hydrogen chloride, the salt recrystallized twice from a mixture of equal volumes of concentrated hydrochloric acid, glacial acetic acid, and water (activated charcoal) and then decomposed with aqueous ammonia and the free base recrystallized as given below: from pyridine (twice), from m-xylene (twice) and from benzene (once). After drying in vacuum at 100°, the amine had m.p. 298-299°.

p-Nitroaniline. "Chemically pure" grade material was recrystallized several times from water and benzene and had m.p. 150°.

II. Procedure and Results of Kinetic Measurements

The procedure for measuring the rates of the reactions studied was mainly the same as in the previous work [7]. It consisted of stopping the reaction between the amine and picryl chloride at a definite moment by adding a benzene solution of diethylamine to the mixture and determining the residual aromatic amine by potentiometric titration with sodium nitrite [9]. Due to the specific properties of the amino derivatives of p-terphenyl (low solubility of the 4-amino-4"-nitro derivative in benzene and of the hydrochlorides of both amines in hydrochloric acid), this procedure was modified somewhat. Thus, for example, due to the solubility, it was necessary to measure the reaction rate with a very low initial concentration of 4-amino-4"-nitro-p-terphenyl (b) and, consequently, of picryl chloride also, since in accordance with the reaction scheme, the concentration of the latter substance (a) was half that of the amine, as in previous work [6, 7]. The greatest concentration, b, which we



were able to reach was 0.001 M. For this, 50 ml of 0.0011 M solution of amine was mixed with 5 ml of 0.0055 M picryl chloride solution. Despite its considerable volume, the reaction mixture prepared in this way contained half of the recommended amount of amine for analysis [10], but this did not noticeably affect the accuracy of the measurements.

The reaction was stopped by adding to the reaction mixture 1 ml of a solution consisting of one volume of diethylamine and three volumes of benzene. After 3-5 minutes, 1-2 drops of a 0.1% solution of Methyl Red in glacial acetic acid was added, followed by the dropwise addition of a saturated solution of dry hydrogen chloride in anhydrous ether until the indicator showed an acid reaction. The flask was attached to a distillation condenser and immersed as far as possible in a hot water bath (up to the side arm) and the organic solvent distilled to dryness. To the residue was added 8-10 ml of glacial acetic acid and 0.5-1 ml of concentrated hydrochloric acid. The whole contents of the flask dissolved with gentle heating and the solution was transferred to a titration beaker. The flask was rinsed three times with glacial acetic acid (7-8 ml portions) into the same beaker, to which was then added 2-3 ml of water (to avoid a precipitate) and crystalline potassium bromide, and the aromatic amine determined in the usual way [7-10].

Although 4-amino-p-terphenyl is more soluble in benzene than its 4"-nitro derivative, nonetheless, for a more reliable comparison of the results, the kinetic experiments with the two amines were carried out with the same initial concentration of the reagents (a = 0.0005 m, b = 0.001 m). In the case of 4-amino-p-terphenyl, it was particularly difficult to find conditions for determining the amine as it was found that its hydrochloride had a very low solubility in water and acetic acid. The analysis was only successful with very strict observation of the following conditions. When the reaction had been stopped, the mixture acidified with an ether solution of hydrogen chloride and the solvent evaporated, to convert the 4-amino-p-terphenyl salt into the free base, the dry

TABLE 1

Kinetics of the Reaction of 4-Amino-p-terphenyl with Picryl Chloride, a = 0.0005 m; b = 0.001 m

25°				50°			
t_i (min)	yield (%)	K_i (liter/mole·sec)	n_i	t_i (min)	yield (%)	K_i (liter/mole·sec)	n_i
45	16.6	0.0744	2	20	18.9	0.202	2
100	28.3	0.0661	2	36	29.8	0.204	2
130	34.4	0.0678	2	56	40.6	0.211	2
240	48.3	0.0654	2	84	50.3	0.208	2
360	59.6	0.0686	2	125	58.4	0.194	2
$K_{25°}=0.0685\pm0.0030$				$K_{50°}=0.204\pm0.0006$			

E = 8400 cal/mole; A = $9.2\cdot10^4$ liter/mole·sec.; $\Delta S^{\#}$ = −37.9 cal/°C ·mole.

TABLE 2

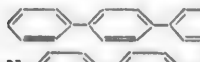
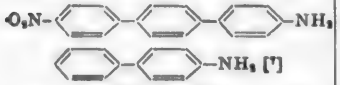
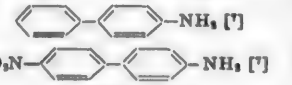
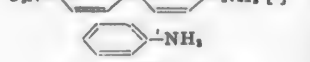
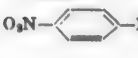
Kinetics of the Reaction of 4-Amino-4"-nitro-p-terphenyl with Picryl Chloride, a = 0.0005 m; b = 0.001 m

25°				50°			
t_i (min)	yield (%)	K_i (liter/mole·sec)	n_i	t_i (min)	yield (%)	K_i (liter/mole·sec)	n_i
120	16.6	0.0328	2	30	16.3	0.112	2
180	24.3	0.0299	2	60	28.2	0.113	2
313	35.9	0.0301	2	95	36.8	0.106	2
580	49.5	0.0284	2	165	48.7	0.0995	2
910	61.5	0.0294	2	264	61.5	0.105	2
$K_{25°}=0.0301\pm0.0013$				$K_{50°}=0.107\pm0.004$			

E = 9700 cal/mole; A = $4.1\cdot10^5$ liter/mole·sec.; $\Delta S^{\#}$ = 34.9 cal/°C ·mole.

TABLE 3

Summarized Data on the Kinetics of the Reactions of Aromatic Amines with Picryl Chloride*

Amine	$K_{25°}$	$K_{50°}$	E	A	$\Delta S^{\#}$
	0.0685±0.0030	0.204±0.006	8400	$9.2\cdot10^4$	−37.9
	0.0301±0.0013	0.107±0.004	9700	$4.1\cdot10^5$	−34.9
	0.0744±0.0021	0.235±0.003	8800	$2.1\cdot10^5$	−36.2
	0.00548±0.00018	0.0205±0.0009	10000	$1.4\cdot10^5$	−37.1
	0.120±0.002	0.394±0.005	9100	$5.6\cdot10^5$	−34.3
	0.0000070 **	0.000041	13500	$5.8\cdot10^4$	−38.9

* The dimensions of the values are the same as in Tables 1 and 2.

** Calculated from data for higher temperatures.

residue was treated with 1 ml of a solution of diethylamine in benzene with the concentration given above and then 5-10 ml of glacial acetic acid and 10 ml of benzene* were added; the whole of the residue dissolved on gentle heating and the solution was quantitatively transferred to a titration beaker (the flask was rinsed 3 times with 5 ml portions of glacial acetic acid). To the solution was added 2 ml of 8% hydrochloric acid, crystalline potassium bromide and 2 ml of distilled water (it was necessary to avoid precipitation and to measure out the liquids accurately) and then the titration carried out.

In measuring the rate of reaction of p-nitroaniline with picryl chloride, we encountered another difficulty: the interaction between these substances proceeded exceptionally slowly. Thus, for example, in the case where a = 0.005 M and b = 0.01 M, even after 5 hours at 25° no noticeable change in the concentration of amine in the reaction mixture could be detected. We were able to record the very low rate of this reaction only at a concentration of p-nitroaniline close to that of a saturated solution and at an elevated temperature. But even in this case (a = 0.0083 M, b = 0.0166 M),** it required 38 hours at 50° and more than 10 hours at 70° for the reaction yield to reach 8%. It is understandable that with such a low yield, a considerable systematic error could arise in the determination of the rate constant, though according to our conjectures, it did not exceed 10%; as will become evident later, this error has no effect on the conclusions of the present work. The procedure for measuring the rate in the last case was the same as in paper [7]. The values found for the rate constants for this reaction were 0.000041 liter/mole · sec. at 50° and 0.00014 liter/mole · sec. at 70°.

We described previously [7] the methods of calculating the kinetic parameters and evaluating their accuracy.

The numerical data obtained for the reactions of 4-amino-p-terphenyl and 4-amino-4"-nitro-p-terphenyl are presented in Tables 1 and 2, where the following notations are used. K_i and K, respectively, are the average values of the rate constants, 1) for a given time interval t_i and at a number of measurements n_i and 2) for all Σn_i measurements, E is the activation energy, A, the frequency factor and ΔS the activation entropy. In these tables the second column gives the average values of the reaction yields for n_i measurements.

Table 3 gives the main results on the kinetics of the reactions investigated in the present work and also certain values for the reactions we studied previously.

DISCUSSION OF RESULTS

Comparison of the reaction rates for aniline, 4-aminobiphenyl, and 4-amino-p-terphenyl (Table 3) shows that the electronic effect of such para-substituents as biphenyl and phenyl groups, introduced into the aniline molecule, is almost the same quantitatively and qualitatively. This is most likely explained by the fact that in the molecule of 4-amino-p-terphenyl the benzene nucleus furthest removed from the amino group has no essential effect on the latter.

TABLE 4

Value of f Factors for the Molecular Systems of Benzene, Biphenyl, p-Terphenyl, and Trans-Stilbene

System	$f_{25°}$
	17143
	13.6
	2.28
[7]	5.11

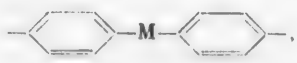
Table 4 gives the f factors for the molecular systems of benzene, biphenyl, and p-terphenyl. These data show that the effect of the nitro group on the reactivity of an amino group in a benzene system is exceptionally strong. The effect of the nitro group is considerably weakened if it is separated from the amino group by a system of two benzene nuclei and becomes quite insignificant when separated from this group by three benzene nuclei. The considerable decrease noted in the effect of the nitro group on the reactivity of the amino group in the case considered should be explained by a fall in conductivity with respect to the electronic interaction of substituents in the nuclear systems of benzene, biphenyl and p-terphenyl both due to the increase in the separation of the extreme para-positions

*Naturally, this amount of benzene can be left during the evaporation.

**These concentrations were obtained by mixing 5 ml of a 0.02 M solution of p-nitroaniline with 1 ml of a 0.05 M solution of picryl chloride.

in these systems and also because the planes in the directly attached benzene nuclei in them must have an non-coplanar steric configuration [11-15]. Besides the steric structure of these systems, attention should also be paid to the fact that the transfer of the electronic effect of the substituents from one benzene nucleus to another here may be hindered due to the high stability of the benzene electronic systems[16] (cf. [2]).

In some previous communications in this series [3-5, 7], we studied the character of the interaction of para-substituents in systems of the form



where M is a bridge grouping attached to two benzene nuclei. In particular, it was established (Table 4) that the molecular system of trans-stilbene, in which M = −CH=CH−, is a poorer transmitter of the electronic effect of substituents than the biphenyl system where the benzene nuclei are directly attached to each other. From this point of view, the bridging phenylene grouping in the molecular system of p-terphenyl hinders the interaction of para-substituents in the different benzene nuclei attached to it even more than the vinylene bridge in the stilbene systems.

As regards the energy indices of the reactions examined in the present work, we will confine ourselves to stating that they are characterized by noticeably smaller changes in the activation entropies than in the activation energies.

SUMMARY

1. A study was made of kinetics of the reactions of 4-amino-p-terphenyl, 4-amino-4"-nitro-p-terphenyl and p-nitroaniline with picryl chloride in benzene solution; the results obtained were compared with kinetic data for the similar reactions of aniline and 4-amino- and 4-amino-4'-nitro derivatives of biphenyl and trans-stilbene.

2. It was shown that the nitro group has a powerful effect on the reactivity of an amino group in the para-position of the same benzene nucleus. This effect is considerably decreased in the binuclear molecular system of biphenyl and almost disappears in the p-terphenyl system, which consists of three benzene nuclei. The phenomenon noted is explained by the peculiarities of the steric structure of such aromatic systems.

3. The bridging phenylene grouping between the benzene nuclei in the p-terphenyl molecular system transmits the electronic effects from one nucleus to another not as well as the vinylene grouping in the trans-stilbene system.

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CYANINE DYES CONTAINING FLUORINE

VIII. SYNTHESIS OF CYANINE DYES FROM 4,6-BIS-(TRIFLUOROMETHYL)-, 4-CHLORO-6-TRIFLUOROMETHYL-, AND 4-CHLORO-6-TRIFLUOROMETHYLSULFONYLBENZIMIDAZOLE

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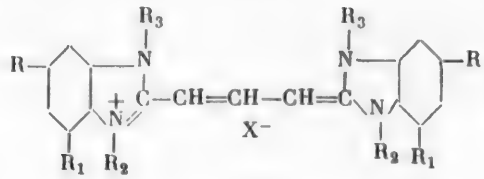
In a previous communication [1], we described the synthesis of imidocarbocyanines containing trifluoromethyl and trifluoromethylsulfonyl groups as substituents in position 6 of the benzimidazole nucleus. In the present work we prepared the tetrasubstituted imidocarbocyanines with the general formula (A).



(A)

$R = R_1 = CF_3$
$R = CF_3$, $R_1 = Cl$
$R = SO_2CF_3$, $R_1 = Cl$
$R = SO_2CF_3$, $R_1 = H$

R_2, $R_3 = CH_3$, C_2H_5, C_6H_5, α-$C_{10}H_7$.
$X = I$ or ClO_4.

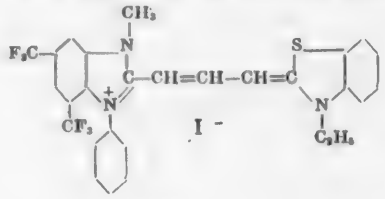
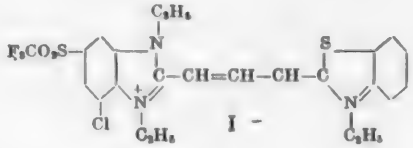
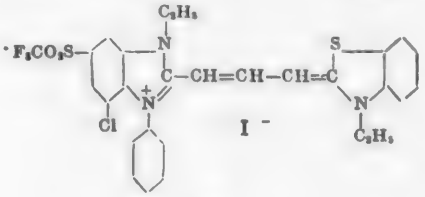
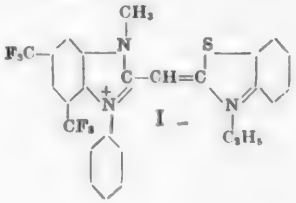
The benzimidazole derivatives and quaternary salts required as starting materials were synthesized by the method described previously [1]. The formulas and absorption maxima in alcohol of the symmetrical dyes obtained are presented in Table 1. For comparison we give the absorption maxima of the corresponding dyes without substituents in position 4 of the benzimidazole nucleus.

TABLE 1

Dyes of General Formula (A)

Dye No.	R	R_1	R_2	R_3	X	λ_{max} (mμ): dye with substituent R_1 in position 4	λ_{max} (mμ): same dye without substituent in position 4
I	CF_3	CF_3	C_2H_5	C_2H_5	I^-	520	507
II	CF_3	CF_3	C_6H_5	CH_3	I^-	516	504
III	CF_3	CF_3	C_6H_5	C_2H_5	I^-	522	511
IV	CF_3	Cl	C_6H_5	C_2H_5	ClO_4^-	515	511
V	SO_2CF_3	Cl	C_2H_5	C_2H_5	I^-	528	522
VI	SO_2CF_3	Cl	C_6H_5	CH_3	I^-	522	518
VII	SO_2CF_3	Cl	C_6H_5	C_2H_5	I^-	528	525
VIII	SO_2CF_3	H	α-$C_{10}H_7$	CH_3	ClO_4^-	—	514

TABLE 2

Dye No.	Formula	λ_{max} (in mμ)
IX		535
X		538
XI		542
XII		418

As the data in Table 1 show, the introduction of trifluoromethyl groups into the 4,4'-positions of 6,6'-bis-(trifluoromethyl)-imidocarbocyanines (dyes I-III) produced a shift in the absorption maximum toward longer wavelengths by 11-13 mμ and the introduction of a chlorine atom into the same position, a shift of only 4 mμ (dye IV) and from 3 to 6 mμ in 6,6'-bis-(trifluoromethylsulfonyl)-imidocarbocyanines (dyes V-VII).

Table 2 gives the formulas and absorption maxima of four unsymmetrical cyanine dyes.

The introduction of a further trifluoromethyl group apparently makes the basicity of the benzimidazole nucleus similar to that of the benzthiazole nucleus – the hypsochromic shift of the absorption maximum (deviation from the arithmetic mean of the two mother dyes) was only 2 mμ (dye IX) instead of 11 mμ for the 6-trifluoromethyl substituted dye and 5 and 1 mμ, respectively, for the 6-trifluoromethylsulfonyl-4-chloro derivatives (dyes X and XI).

EXPERIMENTAL

4-Chloro-5-nitro-1,3-bis-(trifluoromethyl)-benzene was obtained from 4-amino-1,3-dimethylbenzene, in which the amino group was replaced by chlorine by Sandmeyer's method, the side chain chlorinated at 130-150° in ultraviolet light [2], the chlorine replaced by fluorine by means of antimony trifluoride and the product obtained nitrated [3].

2-Nitro-4,6-bis-(trifluoromethyl)-diphenylamine. 5.12 g of 4-chloro-5-nitro-1,3-bis-(trifluoromethyl)-benzene and 10.24 g of aniline were heated on an oil bath for 4 hours at 100-120° and 20 minutes at 140°. To the cooled reaction mixture was added 10% hydrochloric acid and the precipitate collected and washed with 10% hydrochloric acid and water. After recrystallization from aqueous methyl alcohol, the product was obtained in a yield of 4.61 g (75.5%) and had m.p. 112-113°.

Found %: N 8.25, 7.79. $C_{14}H_8O_2N_2F_6$. Calculated %: N 8.02.

2-Amino-4,6-bis-(trifluoromethyl)-diphenylamine. 7 g of 2-nitro-4,6-bis-(trifluoromethyl)-diphenylamine was mixed with 30 ml of methyl alcohol and heated on a boiling water bath for 2 hours with a solution of 16 g of stannous chloride in 16 ml of concentrated hydrochloric acid. When the product had been recrystallized from aqueous methyl alcohol, the yield was 5.67 g (88.6%) and the m.p. 99-100°.

Found %: N 8.53, 8.45. $C_{14}H_{10}N_2F_6$. Calculated %: N 8.75.

2-Methyl-3-phenyl-4,6-bis-(trifluoromethyl)-benzimidazole. A solution of 3.4 g of 2-amino-4,6-(trifluoromethyl)-diphenylamine in 8 ml of benzene was mixed with a solution of 1.8 g of acetyl chloride in 2 ml of benzene and boiled for 2 hours. The benzene was removed and the product dissolved in dilute hydrochloric acid. The base was precipitated with ammonia. It was recrystallized from aqueous methyl alcohol. The yield was 3.13 g (86.0%) and the m.p. 153°.

Found %: N 8.00, 7.85. $C_{16}H_{10}N_2F_6$. Calculated %: N 8.01.

5-Nitro-4-ethylamino-1,3-bis-(trifluoromethyl)-benzene. 5 g of 5-nitro-4-chloro-1,3-bis-(trifluoromethyl)-benzene was heated with 9 ml of a 30% alcohol solution of ethylamine in a sealed tube for 6 hours at 125-130°. The reaction mixture was poured into water and the product extracted with ether. The b.p. was 111-113° (9 mm). The yield was 3.65 g (71.0%).

Found %: N 8.97, 9.03. $C_{10}H_8O_2N_2F_6$. Calculated %: N 9.27.

2-Methyl-3-ethyl-4,6-bis-(trifluoromethyl)-benzimidazole. A solution of 4.1 g of 5-nitro-4-ethylamino-1,3-bis-(trifluoromethyl)-benzene in 10 ml of alcohol was mixed with a solution of 10.8 g of stannous chloride in 9 ml of concentrated hydrochloric acid and boiled for 2 hours. The yield of 5-amino-4-ethylamino-1,3-bis-(trifluoromethyl)-benzene was 2.45 g (66.3%) and the b.p. 94-97° at 10 mm. A solution of 2.45 g of the amine obtained in 3 ml of benzene was mixed with a solution of 1.3 ml of acetyl chloride in 2 ml of benzene and boiled for 3 hours. The benzene was removed and the residual oil dissolved with heating in 20% hydrochloric acid and precipitated with ammonia. The product was dissolved in benzene and the benzene removed by distillation. The product was dried in vacuum at 120° and used for preparation of the quaternary salt without further purification.

5-Nitro-4-amino-1,3-bis-(trifluoromethyl)-benzene. 3 g of 5-nitro-4-chloro-1,3-bis-(trifluoromethyl)-benzene was heated with 3 ml of 30% alcoholic ammonia in a sealed tube for 6 hours at 140-150°. The alcohol was removed and the product crystallized from ligroine. The yield was 1.9 g (66.4%) and the m.p. 69-70°.

Found %: N 10.22, 10.28. $C_8H_4N_2O_2F_6$. Calculated %: N 10.22.

4,5-Diamino-1,3-bis-(trifluoromethyl)-benzene. 2.8 g of 5-nitro-4-amino-1,3-bis-(trifluoromethyl)-benzene was dissolved in 10 ml of alcohol and boiled with a solution of 8 g of stannous chloride in 6 ml of concentrated hydrochloric acid for 3 hours. The yield was 1.8 g (72.0%) and the b.p. 98-100° at 10 mm. The product was crystallized from ligroine and had m.p. 48-49°.

Found %: N 11.17, 11.22. $C_8H_6N_2F_6$. Calculated %: N 11.47.

2-Methyl-4,6-bis-(trifluoromethyl)-benzimidazole. A mixture of 0.5 g of 4,5-diamino-1,3-bis-(trifluoromethyl)-benzene, 0.9 ml of acetic anhydride and 1.8 ml of 20% hydrochloric acid was boiled for 2 hours. The base was precipitated with ammonia. When the product had been recrystallized from aqueous alcohol, the yield was 0.45 g (82.0%) and the m.p. 204-205°.

Found %: N 9.59, 9.73. $C_{10}H_6N_2F_6 \cdot H_2O$. Calculated %: N 9.79.

It was shown that water of crystallization was present.

The 3-amino-4-chlorophenyl trifluoromethyl sulfone used had m.p. 94-95° [4].

3,4-Dichlorophenyl trifluoromethyl sulfone. 2.9 g of 3-amino-4-chlorophenyl trifluoromethyl sulfone was mixed with 30 ml of 60% sulfuric acid, heated with stirring to 98°, cooled gradually to 0° and diazotized at this temperature with a solution of 1.1 g of sodium nitrite in 2 ml of water. Stirring was continued for 1 hour. The solution of diazonium salt was filtered and poured into a cooled solution of 1.11 g of cuprous chloride in 10 ml of hydrochloric acid. The mixture was left overnight and then steam distilled. The product was recrystallized from alcohol. The yield was 2 g (64.0%) and the m.p. 52-53°.

Found %: Cl 25.28, 25.48. $C_7H_3O_2SCl_2F_3$. Calculated %: Cl 25.44.

3-Nitro-4,5-dichlorophenyl trifluoromethyl sulfone. 3.06 g of 4,5-dichlorophenyl trifluoromethyl sulfone was mixed with 11.1 ml of nitric acid (d 1.5) and 22.6 g of 30% oleum. The mixture was stirred for 3 hours at 110°. It was poured onto ice. When the product hadbeen recrystallized from methyl alcohol, the yield was 2.3 g (64.8%) and the m.p. 83-84°.

Found %: N 4.58, 4.54. $C_7H_2O_4NSCl_2F_3$. Calculated %: N 4.32.

2-Chloro-4-trifluoromethylsulfonyl-6-nitrodiphenylamine. 4.12 g of 3-nitro-4,5-dichlorophenyl trifluoromethyl sulfone and 8.24 g of aniline were heated on an oil bath for 4 hours at 130°. The precipitate was transferred into a 10% solution of hydrochloric acid. The product was collected and washed with water. When the substance had been recrystallized from alcohol, the yield was 4.12 g (85.0%) and the m.p. 145-146°.

Found %: N 6.90, 6.94. $C_{13}H_8O_4N_2SClF_3$. Calculated %: N 7.16.

2-Chloro-4-trifluoromethylsulfonyl-6-aminodiphenylamine. A mixture of 4.73 g of 2-chloro-4-trifluoromethylsulfonyl-5-nitrodiphenylamine and 15 ml of methyl alcohol was boiled with a solution of 9.5 g of stannous chloride in 7.2 ml of concentrated hydrochloric acid for 3 hours. The yield was 3.5 g (80.5%) and the m.p. 173-174°.

Found %: N 7.78, 7.72. $C_{13}H_{10}O_2N_2SClF_3$. Calculated %: N 7.99.

2-Methyl-3-phenyl-4-chloro-6-trifluoromethylsulfonylbenzimidazole. A solution of 3.2 g of 2-chloro-4-trifluoromethylsulfonyl-5-aminodiphenylamine in 3 ml of benzene was mixed with a solution of 1.3 ml of acetyl chloride in 2 ml of benzene and boiled for 3 hours. The benzene was removed. The product was dissolved in hydrochloric acid with heating. The base was precipitated with ammonia. When the product had been recrystallized from aqueous methanol, the yield was 2.73 g (80.5%) and the m.p. 154-155°.

Found %: N 7.52, 7.61. $C_{15}H_{10}O_2N_2SClF_3$. Calculated %: N 7.47.

3-Chloro-4-ethylamino-5-nitrophenyl trifluoromethyl sulfone. A mixture of 1 g of 3,4-dichloro-5-nitrophenyl trifluoromethyl sulfone and 1.55 ml of a 30% alcohol solution of ethylamine was heated in a sealed tube for 6 hours at 100° and for 15 minutes at 120°. The mixture was poured into water. When the product had been recrystallized from methyl alcohol, the yield was 1 g (98.0%) and the m.p. 62-63°.

Found %: N 8.12, 8.17. $C_9H_8O_4N_2SClF_3$. Calculated %: N 8.42.

3-Chloro-4-ethylamino-5-aminophenyl trifluoromethyl sulfone. A mixture of 4.9 g of 3-chloro-4-ethylamino-5-nitrophenyl trifluoromethyl sulfone and 15 ml of alcohol was boiled with a solution of 11.6 g of stannous chloride in 9 ml of concentrated hydrochloric acid. When the product had been recrystallized from aqueous alcohol, the yield was 4 g (90.0%) and the m.p. 110-111°.

Found %: N 8.95, 8.98. $C_9H_{10}O_2N_2SClF_3$. Calculated %: N 9.25.

2-Methyl-3-ethyl-4-chloro-6-trifluoromethylsulfonylbenzimidazole. A solution of 3.7 g of 3-chloro-4-ethylamino-5-aminophenyl trifluoromethyl sulfone in 5 ml of benzene was mixed with a solution of 1.8 ml of acetyl chloride in 2 ml of benzene and boiled for 2 hours. The benzene was removed and the product dissolved in hot 20% hydrochloric acid. The base was precipitated with ammonia. After recrystallization of the product from aqueous methanol, the yield was 3.4 g (86.0%) and the m.p. 134-135°.

Found %: N 8.74, 8.80. $C_{11}H_{10}O_2N_2SClF_3$. Calculated %: N 8.57.

3-Amino-4-chlorobenzotrifluoride was obtained from 3-nitro-4-chlorobenzotrifluoride by the method of Porai-Koshits [5].

3-Nitro-4,5-dichlorobenzotrifluoride. 7 g of 3-amino-4-chlorobenzotrifluoride was ground well with 70 ml of hot 60% sulfuric acid. The mixture was gradually cooled to 0° and diazotized with a solution of 2.53 g of sodium nitrite in 4 ml of water. After 1 hour the solution of the diazonium salt was filtered and poured into a cooled solution of 3.61 g of cuprous chloride in 35 ml of 37% hydrochloric acid. The reaction mixture was left overnight and then steam distilled. The yield was 5 g (65.0%) and the b.p. 63-65° (14 mm).

6.5 g of 3,4-dichlorobenzotrifluoride was mixed with 30 ml of nitric acid (d 1.5) and 60 g of 30% oleum. The mixture was stirred for 3 hours at 100° and for 30 minutes at 110°. The mixture was poured onto ice. The yield was 5.72 g (73.0%) and the b.p. 116-117° at 13 mm.

TABLE 3

Dye (Table 1)	Quaternary salts	Anion	Recrystallization solvent	Yield (in %)	Melting point (with decomp.)	External form of dye	Empirical formula	% I found	% I calc.
I	B	I	$C_2H_5OH + H_2O$	15.4	214—217°	Dark red needles	$C_{29}H_{27}N_4F_{12}I$	16.40, 16.54	16.16
II	F	I		16	265—267	Orange red needles	$C_{35}H_{23}N_4IF_{12}$	14.96, 15.05	14.87
III	A			37.7	233—235	Light red plates	$C_{37}H_{27}N_4IF_{12}$	14.60, 14.57	14.40
IV	E	ClO_4		14.2	246—248	Violet red plates	$C_{35}H_{27}O_4N_4Cl_3F_6$	6.83, 6.87 *	7.11
V	D	I		38.2	228—229	Dark red needles	$C_{27}H_{27}Cl_2O_4N_4S_2IF_6$	14.78, 14.90	14.99
VI	G	I	$CH_3OH + H_2O$	37.7	249—250	Violet red plates	$C_{33}H_{23}O_4N_4S_2Cl_2IF_6$	13.57, 13.61	13.88
VII	C	I		39.3	212—215	Violet red needles	$C_{35}H_{27}O_4N_4S_2Cl_2IF_6$	13.43, 13.55	13.47
VIII	H	ClO_4		26.5	270—273	Dark red needles	$C_{41}H_{29}O_8N_4S_2ClF_6$	6.10, 6.20 *	6.10

* Nitrogen was determined in these experiments.

TABLE 4

Dye (Table 2)	Quaternary salts	Anion	Yield (in %)	Melting point (with decomp.)	External form of dye	Empirical formula	% I found	% I calc.
IX	F	I^-	45	238—240°	Dark red needles	$C_{28}H_{22}N_3SIF_6$	18.60, 18.52	18.87
X	D	I^-	50	214—216	Violet needles	$C_{24}H_{24}O_2N_3S_2ClIF_3$	18.98, 18.74	18.97
XI	C	I^-	50	248—250	Violet red needles	$C_{28}H_{24}O_2N_3S_2ClIF_3$	17.47, 17.49	17.77

Found %: N 5.09, 5.12. $C_7H_2O_2NCl_2F_3$. Calculated %: N 5.38.

2-Nitro-4-trifluoromethyl-6-chlorodiphenylamine. A mixture of 3.77 g of 3-nitro-4,5-dichlorobenzotrifluoride and 7.45 g of aniline was heated for 6 hours at 120°. The product was recrystallized from aqueous ethyl alcohol. The yield was 1.36 g (29.6%) and the m.p. 76-77°.

Found %: N 8.59, 8.54. $C_{13}H_8O_2N_2ClF_3$. Calculated %: N 8.84.

2-Amino-4-trifluoromethyl-6-chlorodiphenylamine. A solution of 1.86 g of 2-nitro-4-trifluoromethyl-6-chlorodiphenylamine in 10 ml of alcohol was mixed with a solution of 4.62 g of stannous chloride in 3.5 ml of hydrochloric acid and boiled for 3 hours. When the product had been recrystallized from aqueous alcohol, the yield was 1.55 g (92.7%) and the m.p. 107-108°.

Found %: N 9.47, 9.55. $C_{13}H_{10}N_2ClF_3$. Calculated %: N 9.77.

2-Methyl-3-phenyl-4-chloro-6-trifluoromethylbenzimidazole. A solution of 1.3 g of 2-amino-4-trifluoromethyl-6-chlorodiphenylamine in 3 ml of benzene was mixed with a solution of 0.7 ml of acetyl chloride in 2 ml of benzene. The benzene was removed and the product dissolved in hot 20% hydrochloric acid. The base was precipitated with ammonia. When the product had been recrystallized from aqueous methanol, the yield was 1.3 g (92.2%) and the m.p. 135-136°.

Found %: N 8.73, 8.86. $C_{15}H_{10}N_2ClF_3$. Calculated %: N 9.01.

The ethyltosylates of 2-methyl-3-phenyl-4,6-bis-(trifluoromethyl)- (A), 2-methyl-3-ethyl-4,6-bis(trifluoromethyl)- (B), 2-methyl-3-phenyl-4-chloro-6-trifluoromethylsulfonyl- (C), 2-methyl-3-ethyl-4-chloro-6-trifluoromethylsulfonyl- (D) and 2-methyl-3-phenyl-4-chloro-6-trifluoromethyl-(E)-benzimidazoles were obtained by heating 1 mole of base with 1.2 moles of ethyl p-toluenesulfonate for 4-5 hours at 140-150°. The quaternary salts solidified on cooling and were washed with ether. The iodides were precipitated from aqueous solutions of the quaternary ethyltosylates with a saturated solution of potassium iodide.

The methylmethosulfates of 2-methyl-3-phenyl-4,6-bis-(trifluoromethyl)-benzimidazole (F), 2-methyl-3-phenyl-4-chloro-6-trifluoromethylsulfonylbenzimidazole (G) and 2-methyl-3-naphthyl-6-trifluoromethylsulfonylbenzimidazole (H) were obtained by heating 1 mole of base with 1.2 mole of dimethyl sulfate for 3 hours at 110°. The product was washed with ether, dissolved in water and the iodide precipitated by the addition of a saturated solution of potassium iodide.

Dyes

All the symmetrical dyes (Table 1) were obtained by heating 1 g of quaternary salt with 1 ml of orthoformic ester and 5 ml of nitrobenzene for 1 hour at 185-190° in the bath. The dyes were precipitated and washed with ether and hot water and recrystallized. Table 3 gives the yields and melting points of the symmetrical imidocarbocyanines.

The unsymmetrical dyes (Table 2) were obtained by boiling 0.001 mole of quaternary salt with 0.001 mole of the ethiodide of 2-ω-acetanilido-vinylbenzthiazole, 5 ml of anhydrous alcohol and 0.001 mole of triethylamine for 2 hours. The dye was collected and recrystallized from aqueous alcohol. Table 4 gives the yields and melting points of the unsymmetrical dyes.

1-Methyl-3-phenyl-4,6-bis-(trifluoromethyl)-benzimidazole-(2)-3'-ethylbenzthiazole-(2')-monomethynecyanine perchlorate (XII). 0.48 g of the methiodide of 2-methyl-3-phenyl-4,6-bis-(trifluoromethyl)-benzimidazole, 0.34 g of the methiodide of 2-methyl-3-ethylmercaptobenzthiazole, 0.1 g of triethylamine and 5 ml of anhydrous alcohol were boiled for 2 hours. The product was recrystallized from aqueous alcohol. It formed yellow needles. The yield was 0.12 g (18.75%) and the m.p. 189-191° (with decomp.).

Found %: I 19.83, 19.75. $C_{26}H_{20}N_3SIF_6$. Calculated %: I 19.62.

SUMMARY

The syntheses of 2-methyl-3-phenyl-4,6-bis-(trifluoromethyl)-, 2-methyl-3-phenyl-4-chloro-6-trifluoromethyl-, and 2-methyl-3-ethyl- and 2-methyl-3-phenyl-4-chloro-6-trifluoromethylsulfonylbenzimidazoles are described. These bases and also 2-methyl-3-α-naphthyl-6-trifluoromethylsulfonylbenzimidazole, which we

described previously, were converted into quaternary salts, from which we obtained 8 symmetrical and 4 unsymmetrical imidocarbocyanines.

Their absorption spectra in alcohol solutions were determined.

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INVESTIGATION IN THE FIELD OF DIECKMANN CYCLIZATION

VII. REARRANGEMENT OF 2-METHYL-2-CARBETHOXYCYCLOHEXANONE INTO 6-METHYL-2-CARBETHOXYCYCLOHEXANONE

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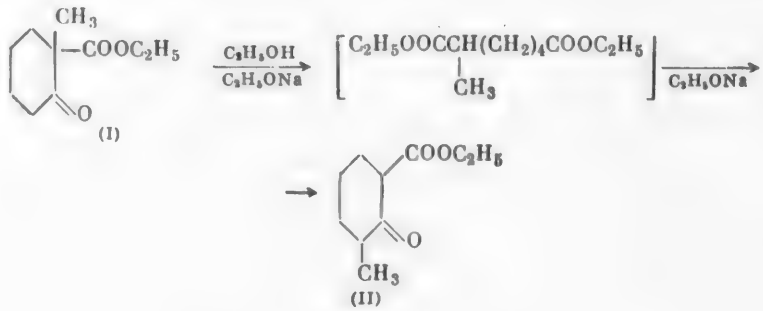
In 1937 a description [1] was given of the rearrangement of 2-(2'-carbethoxyethyl)-2-carbethoxycyclohexanone into 6-(2'-carbethoxyethyl)-2-carbethoxycyclohexanone by boiling with an alcohol solution of 1 mole of sodium ethylate and then this reaction was extended to other 2-(carbethoxyalkyl)-2-carbethoxycyclohexanones [2]. A similar rearrangement was achieved in the cyclopentanone series [3] with 2-(carbethoxymethyl)-2-carbethoxycyclopentanone and in both cases [1, 3] the authors considered that the reaction proceeded through the alcoholysis of the original ester, accompanied by ring opening with subsequent cyclization of the α-(carbethoxymethyl)-alkyldicarboxylic ester formed by the Dieckmann method, but in the other direction. Later Chakravarti [4] proposed a different mechanism for the rearrangement described by Chatterjee et al. [3], but more recently, the opinions of Chakravarti were disproved by a paper [5] demonstrating experimentally that the rearrangement of 2-(carbethoxymethyl)-2-carbethoxycyclopentanone into 5-(carbethoxymethyl)-2-carbethoxycyclopentanone proceeded by the first scheme, i.e. with ring opening and subsequent Dieckmann cyclization.

In view of the fact that the rearrangement of only 2-carbethoxyalkyl derivatives of 2-carbethoxycyclohexanone is described in the literature, it seemed interesting to us to study the analogous rearrangement of a 2-alkyl derivative on the example of 2-methyl-2-carbethoxycyclohexanone (I).

It is known that when (I) is boiled with an alcohol solution of 0.2 mole of sodium ethylate, it smoothly forms the diethyl ester of α-methylpimelic acid [6] and, as we established previously [7], the cyclization of the latter by the Dieckmann method in boiling benzene in the presence of powdered sodium led to 6-methyl-2-carbethoxycyclohexanone (II). However, when the reaction was carried out under normal conditions (an alcohol solution of 1.1 mole of sodium ethylate), we obtained the diethyl ester of α-methylpimelic acid (~40%), unchanged β-ketoester (I) (~20%) and only traces of β-ketoester (II), while when 2-methyl-2-carbethoxycyclohexanone was boiled in xylene in the presence of sodium ethylate, the rearrangement proceeded and (II) was formed in ~42% yield.



It was established that the diethyl ester of α-methylpimelic acid was not cyclized in an alcohol solution of sodium ethylate (the original ester was recovered), while in boiling xylene in the presence of sodium ethylate, the cyclization proceeded smoothly and led to (II) in ~54% yield. These facts and also the formation of a large amount of α-methylpimelic ester in the unsuccessful attempt to carry out the rearrangement of (I) in an alcohol medium conclusively show that the rearrangement of (I) into the corresponding 2,6-analog proceeds with ring opening and subsequent cyclization of the diethyl α-methylpimelate formed by the Dieckmann method.

EXPERIMENTAL

6-Methyl-2-carbethoxycyclohexanone (II). a) From 2-methyl-2-carbethoxycyclohexanone (I). A mixture of 18.4 g of (I) (synthesized according to data in [7]) and a suspension of sodium ethylate (from 3.5 g of powdered sodium and 12 g of anhydrous alcohol) in 100 ml of dry xylene was boiled for 7.5 hours and cooled. The reaction mixture was poured onto 150 g of ice at from 0 to 3° and made acid to Congo with dilute (1:1) hydrochloric acid (~0°), the organic layer separated and the aqueous layer extracted with 50 ml of benzene; the combined xylene-benzene solution was washed successively with 5% sodium carbonate solution (30 ml) and water until neutral to Brilliant Yellow paper, dried over anhydrous sodium sulfate, the solvent removed and the residue vacuum distilled. The yield of (II) was 7.7 g (41.8%):

B.p. 72.5-79.5° (1.5 mm), $n^{20}D$ 1.4720, d^{20}_4 1.0405.

According to literature data: b.p. 84.5-86° (2.5 mm), $n^{20}D$ 1.4720, d^{20}_4 1.0455.

The phenylhydrazone (obtained by the method in [8] in 80.5% yield) had m.p. 136-137° (from 70% alcohol); a mixed melting point with an authentic sample was not depressed.

According to literature data: m.p. 136-138° [8].

b) From diethyl ester of α-methylpimelic acid. Analogously to the above experiment, from 11.5 g of diethyl α-methylpimelate (obtained according to data in [7]) and sodium ethylate (from 1.75 g of powdered sodium and 3.4 g of anhydrous alcohol) in 55 ml of dry xylene, we obtained 5 g (54.3%) of 6-methyl-2-carbethoxycyclohexanone: b.p. 69.5-73° (1.5 mm), $n^{20}D$ 1.4735. The phenylhydrazone (86.5% yield) had m.p. 136-137° (from 70% alcohol).

SUMMARY

1. The rearrangement of 2-methyl-2-carbethoxycyclohexanone into 6-methyl-2-carbethoxycyclohexanone was carried out in the presence of sodium ethylate.

2. It was demonstrated that the reaction proceeded with ring opening and subsequent Dieckmann cyclization of the diethyl ester of α-methylpimelic acid formed.

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INVESTIGATION IN THE FIELD OF ALKANESULFONIC ACIDS

XX. BENZOYLATION OF N-ARYLAMIDES OF ALKANESULFONIC ACIDS

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On the example of the anilide of ethanesulfonic acid, we showed that arylamides of alkanesulfonic acids tend toward substitution reactions at the nitrogen: the hydrogen atom of the NH group is readily replaced by metals and by alkyl, acyl and other residues [1]. In the benzoylation of ethanesulfonoanilide, it was noted that the course of the reaction depended on the conditions: when the anilide was heated with benzoyl chloride at not higher than 150-160° or when the reaction was carried out in a pyridine medium at not more than 116-120°, the N-benzoylanilide was formed according to the equation:

$$RSO_2NHC_6H_5 + C_6H_5COCl \xrightarrow{-HCl} RSO_2N\begin{matrix}COC_6H_5\\ C_6H_5\end{matrix}$$

If the reaction temperature was raised to 200-220°, then so-called transacylation was observed and as a result, the anilide of benzoic acid was formed. This conversion can be illustrated in the following way:

$$RSO_2NHC_6H_5 + C_6H_5COCl \rightarrow C_6H_5CONHC_6H_5 + RCl + SO_2.$$

The purpose of the present work was to study the benzoylation of a series of N-arylamides, namely the anilide of methanesulfonic acid and the toluidides (o- and p-) and anisidides (o- and p-) of methane-, ethane- and butanesulfonic acids. The reaction was carried out under the conditions given above. As the experiments showed, the best results were obtained in a pyridine medium: in this case the N-benzoyl derivatives were formed in higher yields and were purer. The reaction at 200-220° was carried out only with the p-anisidides of ethane- and butanesulfonic acids. In this case transacylation was observed with the formation of the anisidide of benzoic acid and traces of the N-benzoylanisidides of ethane- and butanesulfonic acids, respectively, were also isolated.

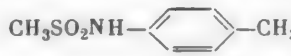
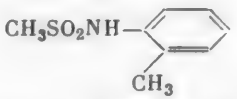
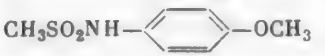
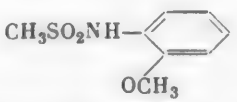
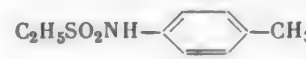
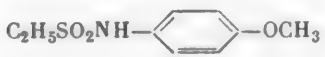
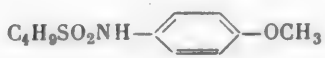
Thus, by benzoylation it is possible to convert N-arylamides of alkanesulfonic acids to N-arylamides of benzoic acid under certain temperature conditions (200-220°). As was found, at this temperature the N-arylamides of alkanesulfonic acids become unstable and as a result of this they decompose with the formation of the more thermostable N-arylamides of benzoic acid.

Considering that benzoylation proceeds at 140-150° and transacylation at 200° and above, we put forward the hypothesis that the latter proceeds in two stages by the following scheme:

$$RSO_2NHAr + C_6H_5COCl \rightarrow RSO_2N\begin{matrix}COC_6H_5\\ Ar\end{matrix} + HCl,$$

$$RSO_2N\begin{matrix}COC_6H_5\\ Ar\end{matrix} + HCl \rightarrow C_6H_5CONHAr + SO_2 + RCl,$$

i.e., normal benzoylation of the original N-arylamide occurs first and then under the action of the high temperature and HCl, the product formed is cleaved according to the scheme presented. This conversion scheme is

Expt. No.	Formula of starting N-arylamide	Taken for reaction: N-arylamide (in g)	Taken for reaction: C_6H_5COCl (in ml)	N-Benzoyl derivatives	Melting point	Yield (in %)	% N: found	% N: calc.	% S: found	% S: calc.
1	$CH_3SO_2NHC_6H_5$	0.4	0.4	Methanesulfono-N-benzoylanilide $C_{14}H_{13}O_3NS$	134—136°	93.75	4.95	5.09	11.48	11.63
2		0.5	0.5	Methanesulfono-N-benzoyl-p-toluidide $C_{15}H_{15}O_3NS$	128—129	84.41	4.80	4.84	11.20	11.03
3		1.0	1.0	Methanesulfono-N-benzoyl-o-toluidide $C_{15}H_{15}O_3NS$	88—89	56.7	4.73	4.84	10.96	11.03
4		0.5	0.45	Methanesulfono-N-benzoyl-p-anisidide $C_{15}H_{15}O_4NS$	115—116	73.33	4.51	4.59	10.58	10.50
5		0.5	0.45	Methanesulfono-N-benzoyl-o-anisidide $C_{15}H_{15}O_4NS$	156—158	93.33	4.66	4.59	10.65	10.50
6		0.4	0.35	Ethanesulfono-N-benzoyl-p-toluidide $C_{16}H_{17}O_3NS$	133—134	89.31	4.57	4.62	10.39	10.56
7		2.0	2.0	Ethanesulfono-N-benzoyl-p-anisidide $C_{16}H_{17}O_4NS$	112—113	71.81	4.37	4.38	9.71	10.03
8		2.0	1.8	Butanesulfono-N-benzoyl-p-anisidide $C_{18}H_{21}O_4NS$	75—76	70.42	3.91	4.03	9.26	9.22

supported by the fact that the reaction in pyridine, which binds the HCl liberated during acylation, proceeds normally with the formation of an individual product with a sharp melting point, while the reaction without pyridine leads to the same product, but with an indefinite melting point. Apparently partial transacylation begins at a lower temperature (140-160°) and this is the reason for the low melting point of the N-benzoylarylamide.

The N-benzoyl-N-arylamides of alkanesulfonic acids obtained were colorless, crystalline substances, which did not dissolve in water and alkali, but were soluble in alcohol and other organic solvents and were without taste, in contrast to N-benzoylamides of alkanesulfonic acids of the general formula $RSO_2NHCOC_6H_5$, whose lower homologs have an intensely sweet taste [2].

EXPERIMENTAL

The same benzoylation procedure was used in all cases. A general description of it is therefore given below and the actual data on each compound are presented in the general table.

a) Benzoylation in a pyridine medium. A definite amount of the N-arylamide was dissolved in pyridine and to the solution was added an excess of approximately one and a half times the calculated amount of benzoyl chloride. The reaction mixture was gently boiled (115-120°) under reflux on a sand bath for 3-4 hours. After the reaction, the mixture was cooled and then made acid with dilute hydrochloric acid. The reaction product precipitated from the acid medium as a solid, greyish mass, which was treated with dilute alkali to remove unreacted arylamide and benzoic acid, formed from benzoyl chloride when the reaction mixture was treated with aqueous hydrochloric acid. The alkali-insoluble N-benzoylarylamide was separated, washed with water, dried, and weighed. The substance was recrystallized from aqueous alcohol.

b) Benzoylation in the absence of pyridine. The reaction was carried out similarly to the above, but in the absence of pyridine and at 140-160°. After the reaction, the mixture was left for a day at room temperature and then transferred to a porcelain basin, where it rapidly set to a hard, solid mass. Subsequent processings and isolation of the reaction product were as described above.

c) Transacylation of anisidides. 2 g of ethanesulfono-p-anisidide and 2 ml of benzoyl chloride (an excess of one and a half times the calculated amount) were heated for two hours in a flask with a reflux condenser on a sand bath at 200-220°, when considerable tar formation was observed. The mixture solidified on cooling and the solid product was treated with alcohol, the carbonized particles removed by filtration and the product precipitated from the alcohol solution with water. We isolated 1.81 g of a substance with an indefinite melting point from 135-147°, which indicated its inhomogeneity. A qualitative analysis showed the presence of nitrogen and very small traces of sulfur. Three fractional crystallizations from alcohol yielded a nitrogen-containing product with m.p. 150-153°, which corresponded to the p-anisidide of benzoic acid (m.p. 154° [3]). A nitrogen analysis also confirmed this conclusion (nitrogen found, 6.21%, calculated, 6.16%). The alcohol filtrates after isolation of the benzanisidide yielded a very small amount of the N-benzoyl-p-anisidide of ethanesulfonic acid with m.p. 109-111° (melting point of pure preparation 111-113°). The nitrogen and sulfur analyses also corresponded to this compound. The benzoylation of the p-anisidide of butanesulfonic acid under the same conditions also formed the p-anisidide of benzoic acid with a very small amount of butanesulfono-N-benzoyl-p-anisidide, which were separated by the method described. A list of the compounds obtained, the amounts of starting materials, and yields and constants of the reaction products are given in the table.

SUMMARY

1. The benzoylation of some N-arylamides of alkanesulfonic acids under different conditions was studied.

2. On the example of the anisidides of ethane- and butanesulfonic acids, it was shown that transacylation of the reaction products occurred at 200-220° with the formation of the anisidide of benzoic acid.

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DERIVATIVES OF BENZ-(c,d)-INDOLINE

III. 1-METHYL-2-METHYLTHIOBENZ-(c,d)-INDOLINIUM SALTS AND THE PRODUCTS OF THEIR CONDENSATION WITH COMPOUNDS CONTAINING AN ACTIVE METHYLENE GROUP

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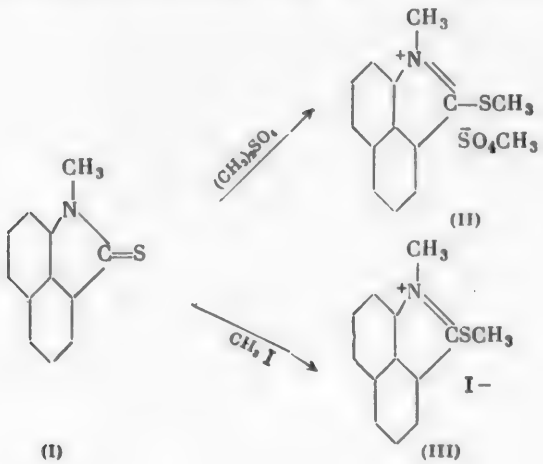
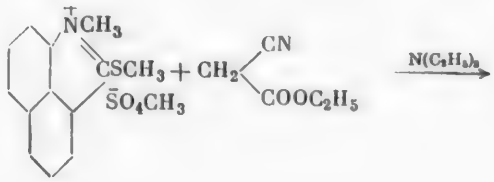
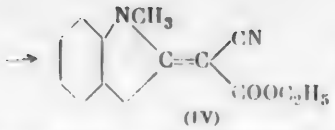
By condensation of thionaphthostyryl with substances containing an active methylene group, one of us obtained a peculiar type of colored compound, partly reminiscent of indigoids, indogenides, and merocyanines [1]. To synthesize compounds of analogous structure, where the hydrogen at the nitrogen is replaced by a methyl group, a method was used which had been developed by Kendal for other heterocyclic compounds [2].

When reacted with dimethyl sulfate, the previously described [3] N-methylthionaphthostyryl [1-methyl-2-thionebenz-(c,d)-indoline] (I) gave a good yield of 1-methyl-2-methylthiobenz-(c,d)-indolinium methylsulfate (II), which was a very unstable compound and decomposed with even traces of moisture to liberate methyl mercaptan. The more stable iodide (III) was obtained from (I) by the action of methyl iodide.



The quaternary salts readily condensed with compounds containing an active methylene group to form colored substances. Heating (II) with ethyl cyanoacetate in anhydrous alcohol in the presence of triethylamine yielded yellow 2-cyano-2-carbethoxymethylene-N-methylbenz-(c,d)-indoline (IV) (λ_{max} 454 mμ, ε $1.85 \cdot 10^4$).

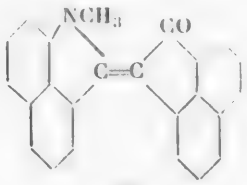




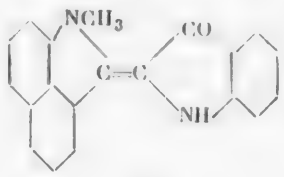
(IV)

$+ CH_3SH + CH_3SO_4H \cdot N(C_2H_5)_3$.

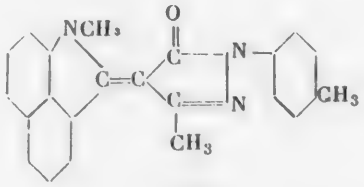
Condensations with acenaphthenone and indoxyl under analogous conditions yielded violet substances, namely, 2-(1-acenaphthanyliden-2-one)-N-methylbenz-(c,d)-indoline (V) (λ_{max} 544 mμ, ϵ $1.97 \cdot 10^4$) and 2-(2-indolinyliden-3-one)-N-methylbenz-(c,d)-indoline (VI) (λ_{max} 548 mμ, ϵ $2.47 \cdot 10^4$) and condensation with 1-p-tolyl-3-methylpyrazol-5-one gave a black-brown product, 2-(1-p-tolyl-3-methyl-4-pyrazolyliden-5-one)-N-methylbenz-(c,d)-indoline (VII) (λ_{max} 476 mμ, ϵ $1.25 \cdot 10^4$).



(V)

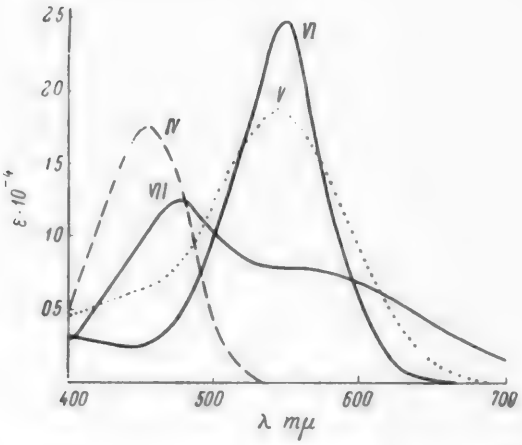


(VI)



(VII)

All the substances were insoluble in water and readily soluble in organic solvents, but none gave "vat" with an alkaline solution of sodium hydrosulfite. Acetate fibers were dyed by an aqueous suspension.



Light absorption of substances (IV), (V), (VI) and (VII). Solution in m-xylene, SF-2M spectrophotometer.

The light absorption of m-xylene solutions of the substances synthesized is given in the figure. A comparison of the light absorption of (V) with that of 1-acenaphtheneindigo (λ_{max} 552 mμ according to our measurements) shows that replacement of the 3-hydroxyindole residue by 1-methylbenz-(c,d)-indoline leads to a hypsochromic shift in the absorption maximum by 8 mμ. This shift is illustrated even more noticeably by a comparison of (VI) with indigo (λ_{max} in m-xylene 595 mμ [4]).

EXPERIMENTAL

1-Methyl-2-methylthiobenz-(c,d)-indolinium methylsulfate (II). 1.6 g of N-methylthionaphthostyryl and 1.46 g of dimethyl sulfate were boiled for 1 hour in 15 ml of toluene and cooled and the product collected, washed with ligroine and dried in vacuum. We obtained 2.4 g (92% of (II). The orange needles (from toluene) had m.p. 117.0-120.0° (decomp.). They were insoluble in benzene and toluene, soluble in boiling alcohol and decomposed by water with the liberation of methyl mercaptan.

1-Methyl-2-methylthiobenz-(c,d)-indolinium iodide (III). 1.5 g of N-methylthionaphthostyryl and 7.5 g of methyl iodide were kept at room temperature for 24 hours. The product was collected by filtration, washed with ligroine and ethyl ether and dried in vacuum. The yield of (III) was 2.4 g (93%). The red-brown crystals (from toluene) had m.p. 116.0-117.5°. They were insoluble in benzene, ligroine and ethyl ether, soluble in alcohol, and decomposed by water.

Found %: N 4.14, 4.19; S 9.41, 9.34. $C_{13}H_{12}NSI$. Calculated %: N 4.10; S 9.38.

Condensation of (II) with ethyl cyanoacetate. 0.7 g of (II), 0.31 g of ethyl cyanoacetate, 0.27 g of triethylamine, and 6 ml of anhydrous alcohol were boiled for 1 hour, 10 ml of water added and the mixture filtered when cool. We obtained 0.40 g (66%) of product. Five recrystallizations from 30% alcohol yielded 0.15 g of (IV) as

yellow needles (from dilute alcohol) with m.p. 111.5-113.0°. The product was readily soluble in alcohol and benzene and dyed acetate fiber a golden yellow color.

Found %: C 73.06, 72.90; H 5.34, 5.37; N 10.07, 10.04. $C_{17}H_{14}O_2N_2$. Calculated %: C 73.40; H 5.03; N 10.07.

Condensation of (II) with acenaphthenone. 0.77 g of (II), 0.40 g of acenaphthenone, 0.30 g of triethylamine and 6 ml of alcohol were boiled for 1 hour. The reaction mixture was diluted with 15 ml of water, cooled and filtered. The yield was 0.60 g (73.5%). The product was dissolved in benzene, purified on a chromatography column packed with Al_2O_3 (eluted with benzene with a few drops of alcohol added to 100 ml of benzene) and recrystallized from benzene. We obtained 0.32 g of (V) as black-brown crystals (from benzene) with m.p. 179.5-181.0°. The product was readily soluble in alcohol and benzene and dyed acetate fiber a red-violet color.

Found %: N 4.27, 4.39. $C_{24}H_{15}ON$. Calculated %: N 4.20.

Condensation of (II) with indoxyl. 0.98 g of (II), 0.60 g of indoxyl (containing 70%) of pure material), 0.38 g of triethylamine and 6 ml of anhydrous alcohol were boiled for 1 hour and cooled and the dye together with precipitated indigo collected by filtration. The precipitate was washed with alcohol and dried. The weight was 0.57 g. The dye was dissolved in benzene by heating. The weight of dye dissolved was 0.40 g (45%) and the benzene insoluble residue (indigo) weighed 0.17 g. The dye was purified by chromatography on Al_2O_3 and recrystallized from benzene. The weight of (VI) was 0.10 g and it formed black-violet crystals (from benzene) with m.p. 215.0-222.0° (decomp.). It was soluble in alcohol and benzene and dyed acetate fiber a violet color.

Found %: C 80.81; H 4.85. $C_{20}H_{14}ON_2$. Calculated %: C 80.56; H 4.70.

Condensation of (II) with 1-p-tolyl-3-methylpyrazol-5-one. 0.70 g of (II), 0.41 g of 1-p-tolyl-3-methylpyrazol-5-one, 0.27 g of triethylamine and 6 ml of alcohol were boiled for 1 hour and cooled and the product collected by filtration and washed with 2-3 ml of alcohol. The yield was 0.60 g (79%). The dye was recrystallized 3 times from 50% alcohol and once from 50% isopropanol. We obtained 0.12 g of (VII) as black-brown crystals (from 50% isopropanol) with m.p. 237.0-238.0°. The dye was soluble in alcohol and benzene and dyed acetate fiber a violet color.

Found %: N 11.70, 11.81. $C_{23}H_{20}ON_3$. Calculated %: N 11.89.

SUMMARY

1. The action of dimethyl sulfate and methyl iodide on N-methylthionaphthostyryl yielded N-methyl-2-methylthiobenz-(c,d)-indolinium methylsulfate and iodide.

2. Condensation of 1-methyl-2-methylthiobenz-(c,d)-indolinium methylsulfate with ethyl cyanoacetate, acenaphthenone, indoxyl,and 1-p-tolyl-3-methylpyrazol-5-one yielded dyes which dyed acetate fiber from aqueous suspensions. The light absorption spectra of m-xylene solutions were measured.

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SOME NITRO AND AMINO DERIVATIVES OF 4,5-DICHLOROACENAPHTHENE

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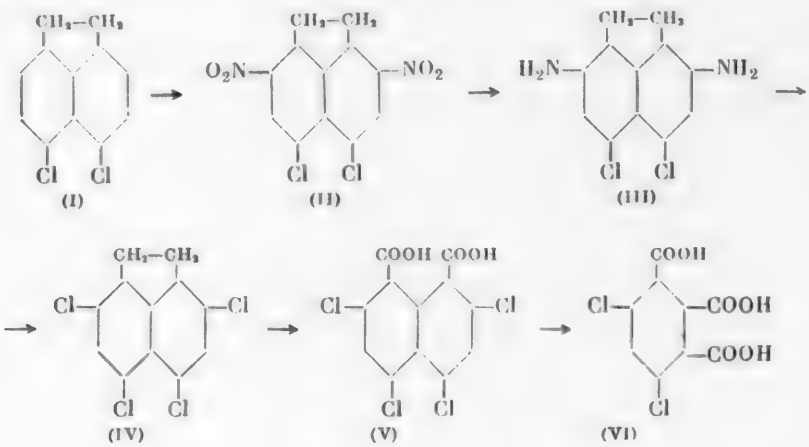
G. Morgan and H. Harrison [1] examined the nitration of 4,5-dichloroacenaphthene (I) and obtained a dichlorodinitroacenaphthene with m.p. 200°. However, they did not establish the structure of this compound or give its yield. We established that the nitration of 4,5-dichloroacenaphthene (I) by the procedure of G. Morgan and H. Harrison yielded dichlorodinitroacenaphthene (II) with m.p. 251-252° (decomp.) in 45-50% yield. By studying the nitration reaction, we were able to raise the yield of product (II) to 72%. The dichlorodinitroacenaphthene (II) obtained was successively converted into dichlorodiaminoacenaphthene (III), tetrachloroacenaphthene (IV), and tetrachloronaphthalic acid (V) and oxidation of the latter gave only 4,6-dichlorohemimellitic acid (VI), which has been described in the literature [2, 3]. The structures of all the compounds we obtained were thus established.



EXPERIMENTAL

4,5-Dichloro-2,7-dinitroacenaphthene (II). 8.92 g of 4,5-dichloroacenaphthene was ground with 6 ml of concentrated sulfuric acid. The paste obtained was introduced with vigorous stirring into 45 ml of 94% nitric acid at such a rate that the temperature was maintained at 2-5° during the whole time. The mixture was poured into 300 ml of water and left for 3-4 hours. The precipitate was collected and washed with water until the acid had been removed, then transferred to a beaker and treated with 100 ml of hot alcohol, filtered again and washed with carbon tetrachloride until the tarry products had been removed completely. We obtained 9 g (72%) of (II). The golden needles (from nitrobenzene) had m.p. 251-252° (with decomp.). They were insoluble in ether, alcohol, and carbon tetrachloride and sparingly soluble in benzene.

Found %: C 45.78, 45.85; H 1.95, 2.01; Cl 22.75, 22.84; N 8.85, 9.10. M 315.4. $C_{12}H_6O_4N_2Cl_2$. Calculated %: C 46.00; H 1.93; Cl 22.65; N 8.95. M 313.

4,5-Dichloro-2,7-diaminoacenaphthene (III). Into a round-bottomed flask with a reflux condenser were placed 9.39 g of well ground (II), 60 g of sodium hydrosulfite, and 200 ml of 50% alcohol. The mixture obtained

was boiled on a water bath for 2 hours, then poured into 200 ml of water and the precipitate collected, washed with water, and dried. The yield of (III) was 7 g (92%) and the m.p. was 229-230°. (III) was freed from small amounts of impurities by conversion to the sulfate and recrystallization from water. Heating the salt with sodium hydroxide solution yielded completely pure (III). It crystallized from alcohol in the form of yellowish brown needles with m.p. 232°. It was sparingly soluble in dilute hydrochloric and sulfuric acids and also in concentrated hydrochloric acid.

Found %: C 56.75, 56.85; H 4.09, 3.85; Cl 27.88, 27.82; N 11.27, 11.15. M 251.5. $C_{12}H_{10}N_2Cl_2$. Calculated %: C 56.91; H 3.96; Cl 28.02; N 11.07. M 253.

The sulfate of (III) was obtained by dissolving the diamine in concentrated sulfuric acid at 40-45° and subsequently diluting the solution with water. The precipitated salt contained only one molecule of sulfuric acid.

Found %: S 9.07, 9.27. $C_{12}H_{12}Cl_2O_4N_2S$. Calculated %: S 9.11.

2,4,5,7-Tetrachloroacenaphthene (IV). 10.53 g of the sulfate of (III) was dissolved in 100 ml of concentrated sulfuric acid at 40-45°, the solution cooled to room temperature and 100 ml of concentrated hydrochloric acid added. The mixture was cooled to 2-3°, a cooled solution of 4 g of sodium nitrite in 100 ml of water added and the mixture stirred for 20-30 minutes. The diazo solution formed was introduced in small portions into a solution of 40 g of cuprous chloride in 200 ml of concentrated hydrochloric acid and stirring continued for 15-20 minutes at 2-3°. The mixture obtained was diluted with 1 liter of water and the precipitate collected, washed with concentrated hydrochloric acid and then water, and dried. The dry product was dissolved in 200 ml of benzene, 20 g of activated charcoal added, and the mixture boiled for 1 hour. The mixture was filtered hot and the charcoal washed with 20 ml of hot benzene. Benzene (170-180 ml) was distilled from the filtrate and the residue left to crystallize. We isolated 5 g (57%) of (IV) with m.p. 216-217°. After many recrystallizations from benzene, the yellowish needles had m.p. 217-218°. They were readily soluble in toluene, xylene, and chlorobenzene and difficultly soluble in alcohol and ether.

Found %: C 49.14, 49.50; H 2.11, 1.99; Cl 48.37, 48.45. M 294.2. $C_{12}H_6Cl_4$. Calculated %: C 49.32; H 2.05; Cl 48.57. M 292.

2,4,5,7-Tetrachloronaphthalic acid (V). 2.92 g of (IV), 130 ml of glacial acetic acid and 10 g of sodium dichromate were introduced into a round-bottomed flask with a reflux condenser and boiled for 1 hour. The reaction mixture was poured into 250 ml of water and filtered. The precipitate was boiled with 6% sodium carbonate solution for 30-40 minutes and filtered. The filtrate was neutralized with hydrochloric acid. This precipitated 0.7 g (20%) of (V). The product crystallized from acetic acid as colorless needles with m.p. 233-234°.

Found %: C 42.71, 43.00; H 0.72, 0.57; Cl 42.08, 42.40. M 338. $C_{12}H_2O_3Cl_4$. Calculated %: C 42.87; H 0.60; Cl 42.23. M 336.

The imide was obtained by heating (V) with a 10% solution of ammonia in the presence of nitrobenzene for 1 hour. The yellow needles (from bromobenzene) had m.p. 269-270°.

Found %: N 4.00, 4.25. $C_{12}H_3O_2NCl_4$. Calculated %: N 4.17.

Oxidation of (V) with potassium permanganate in an alkaline medium by the procedure in [3] formed only 4,6-dichlorohemimellitic acid.

SUMMARY

A procedure was developed for preparing 4,5-dichloro-2,7-dinitroacenaphthene, 4,5-dichloro-2,7-diaminoacenaphthene, 2,4,5,7-tetrachloroacenaphthene, 2,4,5,7-tetrachloronaphthalic acid and its amide, which have not been described in the literature, and the structures of these compounds were proved.

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1-ALKYL-3-METHYL-5-PYRAZOLONES

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As is known, derivatives of 1-aryl-3-methyl-5-pyrazolones find wide application in the production of dyes. In the patent literature there recently appeared a communication on the preparation and use as valuable azo components of new compounds of the pyrazolone series, namely, 1-alkyl-3-methyl-5-pyrazolones, where alkyl = = C_4H_9–C_8H_{17} [1]. These compounds were obtained by the following scheme:

$$RX + NH_2NH_2 \rightarrow RNHNH_2 \xrightarrow[\text{ester}]{\text{Acetoacetic}} CH_3{-}C(=N{-}R){-}CH_2{-}CO$$

However, despite its apparent simplicity, this method is extremely laborious and does not give satisfactory results. In the scheme presented, the most complicated stage is the preparation of the alkylhydrazine. An examination of literature data showed that of the quite numerous methods of synthesizing alkylhydrazines [2, 3], not one offered the possibility of obtaining these compounds by a simple route and in good yields. Therefore, the synthesis method presented above can hardly be considered applicable, especially for the industrial production of dyes.

On the other hand, it is known that 1-alkyl-3-methyl-5-pyrazolones, containing low-molecular alkyls, CH_3–C_4H_9, were obtained by direct alkylation of 3-methyl-5-pyrazolone by the action of alkyl bromides in sealed tubes [4, 5]. We considered that if it were possible to alkylate 3-methyl-5-pyrazolone with higher-molecular alkyl halides in good yields and to simplify the procedure for isolating the products formed, then 1-alkyl-3-methyl-5-pyrazolones would become readily accessible compounds.

It was not necessary to carry out the reaction of 3-methyl-5-pyrazolone with C_5–C_9 alkyl bromides in sealed vessels as the boiling point of the lowest-boiling component was quite high. This made it considerably easier to carry out the reaction. Therefore, we normally carried out the alkylation process by heating the reaction mixture for many hours in a flask with a reflux condenser. Subsequent processing of the reaction mixture was also considerably simplified (see Experimental).

It should be noted that the yields of 1-alkyl-3-methyl-5-pyrazolones depended strongly on the reaction conditions. We studied this dependence in most detail in the synthesis of 1-hexyl-3-methyl-5-pyrazolone, using the same procedure for processing the reaction mixture in all experiments. The effect of reaction temperature on the yield of hexylmethylpyrazolone (heating time 48 hours) was as follows: 125° – 10.2% yield, 135° – 30%, and 140° – 65%. A further increase in temperature led to an increase in the amount of high-boiling products. The effect of reaction time on the hexylmethylpyrazolone yield (reaction temperature 140°) was as follows: 16 hours – 38.5% yield, 25 hours – 43%, 38 hours – 52%, and 48 hours – 65%. The yield of product hardly changed with heating for more than 48 hours. Since it was noticed that the reaction mixture was heterogeneous both before and after the reaction, we considered that the addition of the alcohol with the same radical as the alkyl bromide as a solvent would promote the reaction. Actually, the reaction of 14 g of methylpyrazolone with 22 ml of hexyl bromide (140°, 48 hours) with 10 ml of hexyl alcohol added gave an 85% yield of hexylmethylpyrazolone.

The reaction was carried out similarly in the synthesis of other alkylmethylpyrazolones, but without the selection of the optimal conditions in each separate case. In this way we synthesized the alkylmethylpyrazolones containing alkyls from C_4H_9 to C_9H_{19} (see table).

1-Alkyl-3-methyl-5-pyrazolones Synthesized

Alkyl	Reaction conditions	Yield (in %)	Boiling point (pressure in mm)	Melting point	Analysis results: found (in %)	Analysis results: calc. (in %)	formula
Butyl	130°, 40 hr (in ampoule)	40	126—127° (4)	82—84°	C 62.44, 62.50; H 9.29, 9.12; N 18.27, 18.18	C 62.34; H 9.09; N 18.18	$C_8H_{14}ON_2$
Amyl	140°, 48 (with alcohol added)	58	142—146 (5)	65—68	N 16.83, 16.66	N 16.67	$C_9H_{16}ON_2$
Hexyl		85	151—153 (5)	54—56	C 66.00, 65.87; H 9.95, 9.98; N 15.67, 15.54	C 65.93; H 9.89; N 15.38	$C_{10}H_{18}ON_2$
Heptyl	140°, 48 hr	53	152—154 (4)	56—58	N 14.20, 14.11	N 14.29	$C_{11}H_{20}ON_2$
Octyl		64.5	162—164 (4)	57—59	C 68.39, 68.50; H 10.49, 10.31; N 13.25, 13.16	C 68.57; H 10.48; N 13.33	$C_{12}H_{22}ON_2$
Nonyl		45	166—169 (4)	58—60	N 12.52, 12.37	N 12.50	$C_{13}H_{24}ON_2$

To confirm the structures of the alkylmethylpyrazolones obtained, two of them, namely, 1-hexyl-3-methyl-5-pyrazolone and 1-octyl-3-methyl-5-pyrazolone were obtained by cyclization from the corresponding alkylhydrazines and acetoacetic ester. Mixed melting points of samples of the substances synthesized by different methods were not depressed.

EXPERIMENTAL

3-Methyl-5-pyrazolone was obtained from acetoacetic ester and hydrazine hydrate by the procedure described by V. M. Rodionov and A. M. Fedorova [6]. The yield was 72%.

1-Alkyl-3-methyl-5-pyrazolones were synthesized in the following way: 24.5 g (0.25 mole) of 3-methyl-5-pyrazolone and 0.27 mole of alkyl bromide were heated on an oil bath at 140° for 48 hours (continuously). The cooled reaction mixture was treated with 21 g (0.25 mole) of $NaHCO_3$ and 50 ml of hot water. The mixture was heated on a gently boiling water bath for 1 hour. The product was extracted with ether (ethyl acetate could be used) and the extracts dried with anhydrous sodium sulfate. Vacuum distillation yielded 1-alkyl-3-methyl-5-pyrazolone; the solid product was purified by grinding with heptane, filtration, and vacuum distillation again. The substances obtained and their constants and yields are presented in the table.

Synthesis of 1-alkyl-3-methyl-5-pyrazolones from acetoacetic ester and alkylhydrazines. a) Hexyl hydrazine was obtained by the action of anhydrous hydrazine on hexyl chloride in 23-26% yield; b.p. 74-80° (12-14 mm) [3]. A solution of 26.5 g of hexylhydrazine in 50 ml of alcohol was added dropwise with stirring to a solution of 30 ml of acetoacetic ester in 55 ml of alcohol. Stirring was continued for 1.5 hours at room temperature and then for a further 1 hour with heating on a water bath. The alcohol was removed and to the oily residue was added 350 ml of water. The oil solidified on standing; the solid product was collected, washed with water, dried and vacuum distilled. The b.p. was 146-150° (4 mm). Treatment with heptane yielded 7 g (20%) of 1-hexyl-3-methyl-5-pyrazolone with m.p. 54-56°.

b) Octylhydrazine was obtained in 28.5% yield from anhydrous hydrazine and octyl chloride and had b.p. 108-112° (12 mm) [3]. A solution of 14.4 g of octylhydrazine in 25 ml of alcohol was added dropwise with stirring to a solution of 13 ml of acetoacetic ester in 25 ml of alcohol. The mixture was stirred for 1.5 hours at room temperature and for 1 hour with heating on a water bath. The alcohol was removed and the residue vacuum distilled. We obtained 11.1 g (53.5%) of 1-octyl-3-methyl-5-pyrazolone with b.p. 162-165° (4-5 mm) and m.p. 46-47°. After treatment with heptane, the product had m.p. 56-58°.

SUMMARY

A convenient method is proposed for preparing 1-alkyl-3-methyl-5-pyrazolones by direct alkylation of readily accessible 3-methyl-5-pyrazolone. The structure of the 1-alkyl-3-methyl-5-pyrazolones was confirmed by synthesis.

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INVESTIGATION OF SECONDARY REACTIONS IN RADICAL POLYMERIZATION PROCESSES BY THE FORMATION OF "HYBRID" POLYMERS

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By a study of the molecular weight distributions of synthetic polymers obtained by block polymerization under the action of free radicals, it was shown [1] that together with the main reactions of the initiation, growth and breaking of chains, in free radical block polymerization an essential role could be played by secondary reactions: 1) destruction of polymer chains under the action of free radicals; 2) interchain exchange (including exchange with radicals of the initiator and exchange at the expense of the monomer); 3) cross-linking of completed chains, not leading to the formation of a gel and having the character of the recombination of intermediate activated units. These reactions produce a polymodal distribution with several values for the most probable molecular weights (which cannot be explained by the occurrence of only the main reactions of initiation, growth, and breaking of chains [1]) and also the appearance of high-molecular "tails" in the distributions of diene compounds.

The purpose of the present work was a study of these secondary reactions, their role in polymerization and the relative probability of their occurrence. It was proposed to give a direct demonstration of the existence of these reactions by the preparation of "hybrid" polymers (i.e., graft and block polymers) in model systems. As model systems we chose those in which there is a possibility of the secondary reactions proceeding at a considerable rate. Mixed solutions of two different polymers were used and also solutions of polymers in other monomers; various initiators, sources of primary free radicals, were decomposed thermally in these. Hybrid polymers appearing in such systems are the direct product of secondary reactions.

The following methods were used for identifying and studying the hybrid polymers: 1) measurement of the extinction in the ultraviolet (for hybrid polymers containing a polystyrene block [2]); 2) extraction with various solvents; 3) nephelometric titration [3].

The results of the work confirmed the existence of the above mentioned secondary reactions, which characteristically affect the molecular weight distributions of synthetic polymers obtained by radical polymerization.

EXPERIMENTAL

Polymers. Laboratory samples of polystyrene, polyisobutylene, and butadiene rubber were used. Before use in model systems, these polymers were dissolved to give solutions with concentrations of 1-2 g/100 ml, from which the polymers were then precipitated with a 6-10-fold amount of methyl alcohol to remove stray impurities and initiator residues. After precipitation, the polymers were powdered and dried in vacuum ($\sim 10^{-2}$ mm) to constant weight.

Solvents. The toluene, benzene, ethylbenzene, acetone, methyl ethyl ketone, chloroform, and octane used were analytical and chemically pure grades. The octane and chloroform were further checked for the absence of selective absorption in the ultraviolet in the region of 240-500 mμ. The methanol and ethanol used as precipitants were also checked similarly.

Purification of styrene. Among others, we used the model systems: 1) polyisobutylene + solvent + styrene + + initiator; 2) butadiene rubber + styrene + initiator (in the latter case, the styrene was simultaneously the solvent).

Industrial styrene was freed from inhibitor by the standard procedure [4], in which it was distilled in an atmosphere of purified argon at a pressure of ~20 mm.

Removal of oxygen. As is known, oxygen has a substantial effect on radical processes [5, 6]. We therefore carried out special operations, which made it possible to lower its content in model systems to a level at which it had practically no effect on radical processes. 1) The glass ampoules in which the reactions were performed were heated at 200-250 for ~1 hour while attached to a vacuum system (~10^{-2} mm); the system was then flushed with argon and the ampoules filled in a stream of argon, the contents of the ampoule saturated with argon by having argon bubbled through them for ~30 minutes, the ampoules then hermetically sealed, cooled, and sealed off; 2) in a series of experiments, the solutions were also boiled in an atmosphere of argon at a pressure of ~10^{-1} mm for 3-5 minutes (before freezing); 3) the argon used in the experiments (containing 0.1% oxygen according to specifications) was also passed through copper turnings, reduced with hydrogen and heated to ~500°.

Initiators. As sources of primary free radicals, we used benzoyl peroxide [7, 8], azoisobutyrodinitrile [9] and methyl- and ethylphenyltriazenes [10]. The initiators were recrystallized before use.

Experimental procedure and methods of identifying hybrid polymers. Experiments for studying the destruction and secondary polymerization of two different polymers in solution were carried out in sealed glass ampoules at temperatures at which the initiators decomposed rapidly (at 80°, as a rule, with benzoyl peroxide and azoisobutyrodinitrile and at 100-120° with alkylphenyltriazenes). After the reaction, the polymer was precipitated by the dropwise addition of a ~10-fold amount of precipitant (methanol or ethanol). The polymer was then dried, powdered (to ~1 mm particles), and again dried in vacuum (~10^{-2} mm) to constant weight. After this, the polymer, which usually consisted of a mixture of rubber (polyisobutylene or butadiene rubber) and polystyrene, was extracted with octane in which the rubber dissolved (polystyrene does not even swell in octane). The extract was then centrifuged (to remove mechanically entrained polystyrene) and the ultraviolet absorption spectrum of the extract plotted relative to a control solution of rubber of the same concentration. The control was prepared by the same operations from a mixture of two polymers, without the heating in the presence of initiator. Since the reactions

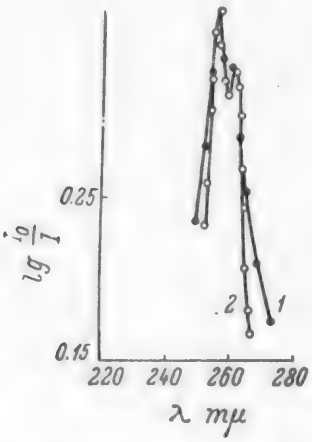

Fig. 1. Selective absorption of octane extract caused by the presence of polystyrene (polyisobutylene + polystyrene + + benzene + methylphenyltriazene system). 1) After a second reprecipitation; 2) after a third reprecipitation.

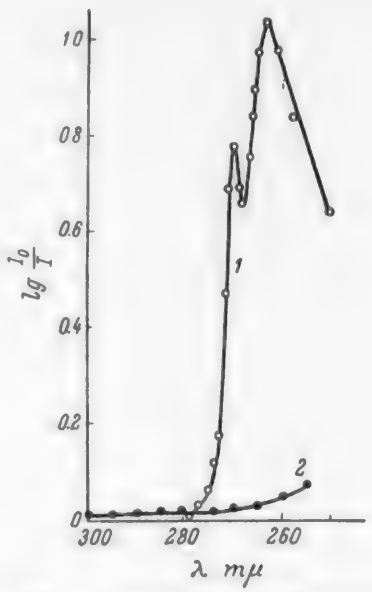

Fig. 2. Selective absorption of polystyrene and absorption of polyisobutylene in chloroform (concentration in both cases, 0.050 g/100 ml). 1) Polystyrene; 2) polyisobutylene.

were carried out in the presence of benzene, ethylbenzene and toluene, which have resonance absorption in the region of 230-270 mμ, one reprecipitation and vacuum drying was found to be insufficient for complete removal of the solvent and the operation was repeated 2-3 times. As experiment showed, the results after the second and third reprecipitations practically coincided (see Fig. 1). The second and third reprecipitations were from octane. According

to our measurements, styrene has selective absorption with maxima in the regions of 262 and 269 mμ in chloroform (agreeing with the data of Melville [2]) with the position of the maximum displaced slightly, depending on the solvent [7] (see Fig. 2). Knowing the specific absorption of polystyrene at 262 or 269 mμ, it was possible to determine the concentration of polystyrene in the hybrid polymer by determining the extinction relative to a solution of polyisobutylene of corresponding concentration, since polyisobutylene does not have selective absorption at these wavelengths and its absorption may be neglected [11] (see also Fig. 2). The specific extinction $\epsilon = E/lc$, where $E = \log\frac{I_0}{I}$ is the absorption found as a reading on the spectrophotometer, l is the length of the light's path through the cell with the solution (in cm) (in our case $l = 1$ cm) and c is the concentration (in g/liter).

From the graph for polystyrene we have:

at the wavelength 269 mμ $\epsilon' = 0.78/1 \cdot 0.5 = 1.56$,
at the wavelength 262 mμ $\epsilon'' = 1.03/1 \cdot 0.5 = 2.06$.

For the case presented in Fig. 1, for example, we find directly that E = 0.4 and λ = 262 mμ and hence the concentration of polystyrene (in g/liter):

$$c = \frac{E}{\epsilon''} = \frac{0.4}{2.06} = 0.194.$$

Since the total concentration of polymer for the measurement was 10 g/liter, then the amount of polystyrene block in the polyisobutylene was in this case

$$\frac{0.194}{10 - 0.194} \approx 2\% \text{ (by weight)}$$

The content of polystyrene blocks in octane extracts in other experiments were calculated analogously. When initiators absorbing ultraviolet light (such as alkylphenyltriazenes and benzoyl peroxide) were used, the rubbers from the reactions showed additional absorption (besides the absorption with maxima at 262 mμ and 269 mμ, caused by polystyrene), which did not disappear on reprecipitation. Thus, for example, in the experiment for which the spectrum of the octane extract is illustrated in Fig. 1, absorption appeared with a maximum in the region of 300 mμ (see Fig. 3). Additional experiments in which polyisobutylene was heated with initiator under the same conditions, but in the absence of polystyrene, showed that absorption appeared with a maximum in the region of 300 mμ (the maxima at ~260-270 mμ did not appear). Apparently, the appearance of this maximum is connected with the introduction into polyisobutylene of an anil radical, which is obtained together with a methyl radical in the thermal decomposition of methylphenyltriazene [10]

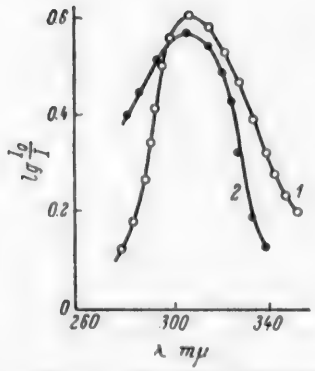

Fig. 3. Selective absorption of polyisobutylene after it had been heated with methylphenyltriazene. 1) Absorption curves after the third precipitation; 2) control curve.

$$C_6H_5—\overset{H}{\underset{|}{N}}—N=N—CH_3 \rightarrow C_6H_5—\overset{N}{\underset{|}{N}}\cdot + CH_3\cdot + N_2,$$

since the $CH_3\cdot$ radical is optically inactive in this region [11] and, according to our measurements, methylphenyltriazene itself has an absorption maximum in the region of 275 mμ.

The other method we used was nephelometric titration [3]. For this purpose we constructed a special apparatus of the type described in the literature [3], but with a multistage Pulfrich photometer instead of photoelements. The temperature of the solution and the precipitant was maintained with an accuracy of ~0.01° by means of a Hëpler ultrathermostat. The concentration of the solutions did not exceed 0.005 g/100 ml. Curves were plotted for the relative turbidity of the system in relation to the amount of precipitant in it. The toluene (solvent) – ethanol (precipitant), octane (solvent) – acetone (precipitant) and benzene (solvent) – methanol (precipitant) systems were used (typical curves are shown in Figs. 7, 9, 10 and 11). If a

dilute solution (~0.005 g/100 ml) of the unfractionated polymer was titrated with precipitant, then a smooth curve was obtained, reflecting the dependence of solubility on molecular weight distribution. If the solution contained a different polymer in addition to the main component, then a break appeared on the nephelometric titration curves (see Fig. 7). Figure 7 shows that in the region of 30% precipitant, the curve of the octane extract is steeper and has a break. Had the solution contained several components, then there would have been several breaks in the curve [3]. This method is a rapid qualitative method of detecting a hybrid polymer in a system.

In a series of cases (especially when insoluble gels were obtained, as with the reaction in a styrene solution of butadiene), a gravimetric control was carried out in addition.

RESULTS AND DISCUSSION

I. Destruction of polymer molecules by free radicals. The possibility of the destruction of polymer molecules in solutions under the action of free radicals has been demonstrated by a series of authors [12-15]. Since

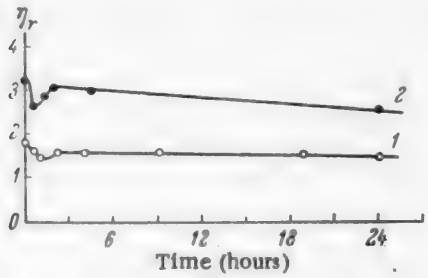

Fig. 4. Dependence of relative viscosity of benzene solutions of polystyrene on time in the presence of methylphenyltriazene (MPT). Concentration of polystyrene in solution: 1) 2 g/100 ml, 120°; 2) 4 g/100 ml, 140°.

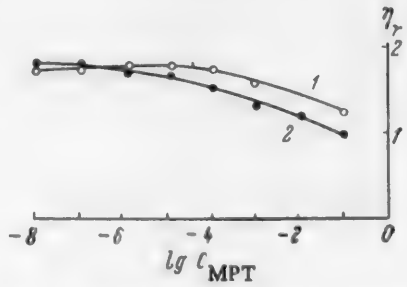

Fig. 5. Dependence of relative viscosity of benzene solutions of polystyrene on MPT concentration. 1) Polystyrene concentration 2 g/100 ml; 2) 4 g/100 ml.

macromolecular recombination and interchain exchange is inconceivable without preliminary destruction of polymer molecules, we carried out a series of preliminary experiments on the destruction of polyisobutylene, polystyrene, and natural and butadiene rubbers, which confirmed literature information on the destructive action of free radicals on polystyrene and rubber. The experiments also showed that strong destruction of rubbers in solutions was also observed in the presence of methyl, ethyl, and benzoyl radicals at low concentrations of initiators (1-2% of the polymer weight). Polystyrene destruction by these radicals was considerably worse and the time dependence of the viscosity change indicated parallel destruction and recombination (see, for example, Fig. 4).* As shown by Fig. 4, the changes in the relative viscosity of the solutions were related to the decomposition of the initiator. The appearance of an initially large amount of radicals caused strong destruction of the polystyrene chains with the appearance of macroradicals. After 1 hour the initiator had decomposed completely and the destruction process practically ceased (spontaneous thermal destruction is very slight at these temperatures), while the recombination process began to dominate, producing an increase in viscosity. Since recombination also apparently occurred during the destruction, here we have a process of repeated recombination and destruction, i.e., interchain exchange. The amount of initiator in this experiment was 0.02-0.04 g/100 ml, i.e., of the same order as is usually used in the initial stages of polymerization. This result was confirmed by an ultracentrifuge study of the molecular weight distribution of a polystyrene sample, which had undergone destruction in the presence of methylphenyltriazene, and this showed that the molecular weight distribution after destruction indicated recombination [1]. The dependence of the relative viscosity of the methylphenyltriazene concentration (Fig. 5)** showed that the destruction proceeded more strongly and began at lower initiator concentrations in the case of more

* In both cases the concentration of MPT was 1% of the concentration of polymer in the solution. The viscosity was measured with an Ostwald viscometer at 25° after dilution with benzene (3-fold).

** Destruction was carried out for 2 hours at 120°. The viscosity was measured at 25° and a concentration of 0.66 g/100 ml.

concentrated polymer solutions and this is apparently connected with the lower mobility of macromolecules in them (i.e., a lower recombination capacity).

II. Formation of hybrid polymers. We observed the formation of hybrid polymers due to secondary reactions in model systems of three different forms.

a) Systems consisting of a mixed solution of two linear polymers without double bonds in the presence of an initiator, a source of free radicals under moderate heating (~100°), namely: 1) mixed solutions of polystyrene and polyisobutylene in toluene with a polymer concentration of 2 g/100 ml (ratio of polystyrene to polyisobutylene of 1 : 1 by weight) in the presence of 2-10% of various initiators (on the polymer weight); 2) mixed solutions of polystyrene (2 g/ 100 ml) and polyisobutylene (0.7 g/100 ml) in benzene in the presence of 2-10% of methylphenyltriazene (on the total polymer weight).

The products obtained in these systems were studied spectrophotometrically. A typical absorption curve of an octane extract obtained in the polystyrene + polyisobutylene + toluene + initiator system [(MPT + Bz_2O_2 in a ratio of 1 : 1 by weight); total concentration of polymers in solution, 2 g/100 ml; concentration of initiators, 1% of concentration of polymers] is presented in Fig. 6. As calculation showed, the polystyrene blocks represented ~10% of the total weight of polymer extracted by octane. In certain cases, nephelometric measurements were carried out to identify the hybrid polymer. Figure 7 shows nephelometric titration curves for the octane extract and a polyisobutylene control; the solvent was octane and the precipitant, acetone. The concentration of the solution for the titration was 0.005 g/100 ml. The polymer was obtained in the polystyrene (2 g/100 ml) + + polyisobutylene (0.7 g/100 ml) + benzene + MPT (10% of the polymer concentration) system. The break in the curve indicates the presence of a hybrid polymer.

Systems of this type are extremely sensitive to various inhibiting impurities and oxygen. If the experiment was carried out without preliminary removal of oxygen, then the octane extract contained only traces of polystyrene. The amount of polystyrene bound to polyisobutylene by secondary reactions in model systems of this type varied from experiment to experiment over the range of 1 to 20% of the total weight of polymer extracted by octane and was 7-10% on the average.

b) Model systems consisting of a solution of polymer in a mixture of solvent and another monomer. Of such systems, we studied: 1) a solution of polyisobutylene in a mixture of toluene and styrene monomer at a concentration of 1 g/100 ml in the presence of methylphenyltriazene (~10% of the polymer concentration); 2) a solution of polyisobutylene in a mixture of ethylbenzene and styrene (1 : 1 by volume) at a concentration of 3 g/100 ml in the presence of various initiators.

The reaction products were studied spectrophotometrically. For systems of this type, the amount of polystyrene blocks in the octane extract did not exceed ~1% of the total polymer (Fig. 8). However, it should be remembered that octane extracts only part of the hybrid polymer, which contains a relatively small amount of polystyrene blocks (as polystyrene is insoluble in octane). Therefore, a considerable part of the hybrid polymer with a predominance of polystyrene had to be dissolved in methyl ethyl ketone (a solvent for polystyrene which does not dissolve polyisobutylene). The presence of hybrid polymer in the methyl ethyl ketone extract obtained from the system polyisobutylene (1 g/100 ml) + toluene + styrene (ratio by volume of 1 : 1 at the beginning of the experiment) + methylphenyltriazene (10% of the polyisobutylene concentration) was shown by the nephelometric titration curve (Fig. 9). As can be seen, curve 3 has a jump in the region of rapid precipitation of polyisobutylene, after which there is a slight increase up to the moment of polystyrene precipitation. The plateau on curve 3 corresponds to turbidity representing ~2.5% of the maximum (100%), indicating that the hybrid polymer in the methyl ethyl ketone extract is also of the order of ~2.5%.

The comparatively low yields of secondary reaction products in the model systems is partly explained by differences in their polymerization conditions (the presence of a large amount of solvent), as a result of which the secondary reactions of destruction and interchain exchange apparently proceed in one act in them.

c) Model systems consisting of a solution of polymer in a different monomer. Of such systems, we studied a 5% solution of butadiene rubber in styrene in the presence of azoisobutyrodinitrile (0.1 g/100 ml), in which the polymerization was carried out at 80-120°. In both cases, both benzene-soluble and benzene-insoluble products were formed. The reaction products were first extracted with benzene (to separate the soluble from the insoluble gel-like products). The polymer extracted by benzene was reprecipitated, dried to constant weight in vacuum, and then extracted with octane and methyl ethyl ketone. The octane extracts were investigated on a spectrophotometer

Fig. 6. Absorption of octane extract (relative to control) after second reprecipitation (concentration 0.05 g/100 ml).

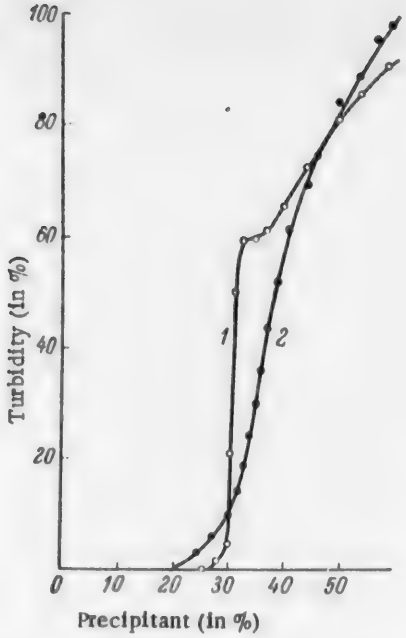

Fig. 7. Nephelometric titration curves for octane extract (1) and polyisobutylene control (2).

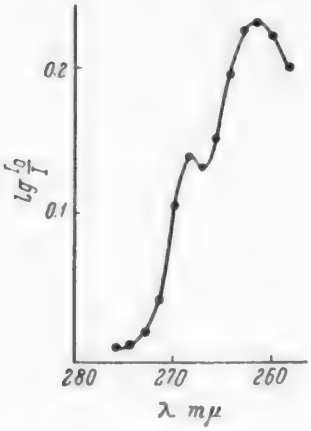

Fig. 8. Absorption of octane extract from the system polyisobutylene (3 g/100 ml) + styrene + ethylbenzene (ratio at beginning of experiment, 1 : 1 by volume) + methylphenyltriazene (15% of polyisobutylene weight).

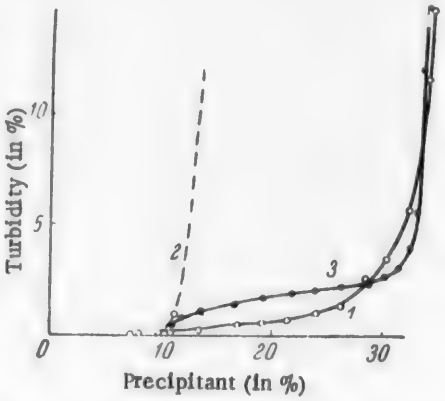

Fig. 9. Nephelometric titration curves of polystyrene extracted from a mechanical mixture of polystyrene and polyisobutylene (1), polyisobutylene (2), and methyl ethyl ketone extract (3). The titration was carried out in a toluene–ethanol system at a polymer concentration of 0.005 g/100 ml.

and by nephelometric titration and the methyl ethyl ketone extracts were investigated nephelometrically.

In addition, a gravimetric control was carried out by the concentrations during extraction with solvents. The results of nephelometric analysis for one of the experiments at 120° are presented below. As can be seen from Fig. 10, the nephelometric curve of the methyl ethyl ketone extract practically coincided with the control curve for polystyrene, indicating the absence of hybrid polymer from the extract. On the other hand, the nephelometric titration curves of the octane and benzene extracts (the latter was obtained after 2-fold extraction with methyl ethyl ketone and octane and therefore must have consisted wholly of hybrid polymer containing such a large

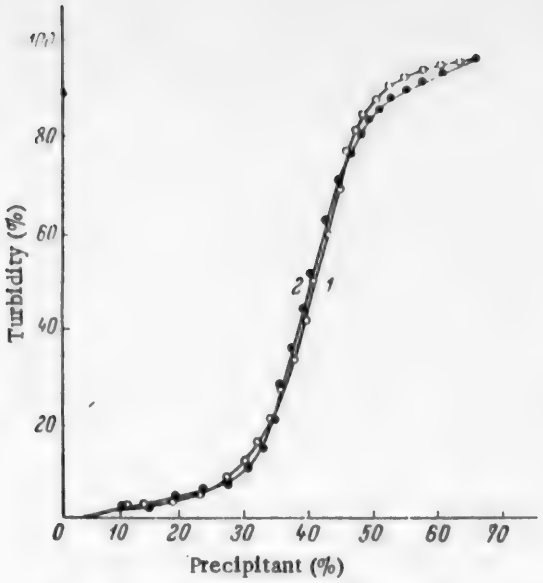

Fig. 10. Nephelometric titration curves of methyl ethyl ketone extract (1) and polystyrene control (2). The measurements were carried out in a toluene – ethanol system at 20° and a polymer concentration of 0.005 g/100 ml.

amount of polystyrene fragments that it was even insoluble in octane) had sharply expressed inflections in the region of ~30% precipitant, corresponding to the beginning of rapid polystyrene precipitation. As can be seen from Fig. 11, the turbidity curve for the benzene extract was displaced in the region of low precipitant concentrations toward the turbidity curve of butadiene rubber solution and in the region of high precipitant concentrations, toward the turbidity curve of polystyrene solution, which, together with the inflection in the region of ~30% precipitant, indicates the hybrid structure of the polymer extracted by benzene. The absence of a hybrid polymer from the methyl ethyl ketone extract and its presence in the octane and benzene extracts apparently indicates the formation in systems of this type of graft polymers with a long diene main chain (hindering their extraction by methyl ethyl ketone) and comparatively short side chains of polystyrene, probably formed due to opening of the double bonds. Gravimetric measurements showed that in model systems of this type at 120°, the weight of the hybrid polymer formed represented ~50% of the weight of butadiene rubber dissolved in styrene, but more than half of this material had a gel structure and was insoluble in

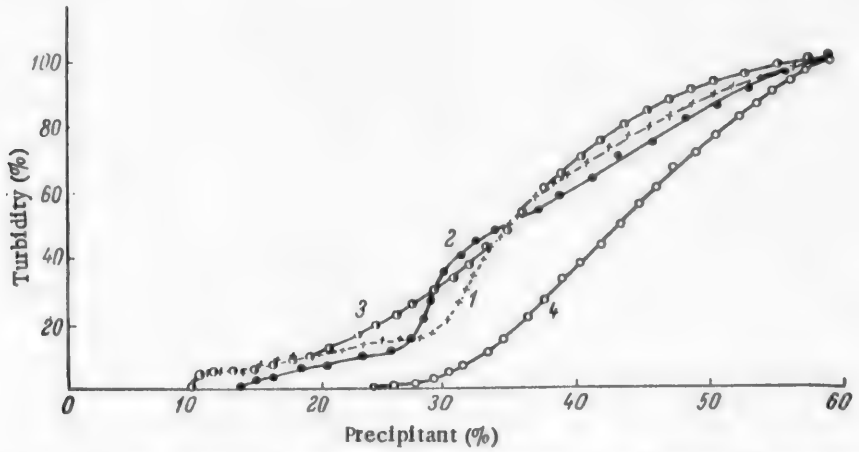

Fig. 11. Nephelometric titration curves of octane (1) and benzene (2) extracts. Control curves for butadiene rubber (3) and polystyrene (4). Explanation in text.

benzene. In analogous experiments at 80°, the weight of hybrid polymer formed represented ~25% on the weight of rubber introduced and in this case, approximately half of the hybrid polymer formed was in the form of a gel.

In conclusion, it should be noted that only the octane extracts were investigated in detail and quantitatively, while the hybrid polymer may either dissolve or not dissolve in octane, depending on the relative amount of the polystyrene part of the macromolecule; therefore, the experiments we performed have a mainly qualitative character.

On the structure of the hybrid polymers formed, it is only possible to form a hypothesis based on the general character of the system. Thus, in mixed solutions of polystyrene and polyisobutylene, block polymers were apparently obtained by destruction with initiators, while the destruction of a solution of polybutadiene rubber in styrene gave graft polymers.

SUMMARY

1. By investigating "hybrid" polymers by a direct method, we demonstrated the presence of secondary reactions of various types, including both the interaction of macroradicals with each other and the interaction of free radicals with polymer chains.

2. An estimation of the yield of hybrid polymers indicated that the reaction which was designated as interchain exchange or macromolecular recombination was less probable than the growth of side branches on diene chains due to the interaction of free radicals with double bonds.

3. The behavior of a newly formed radical after destruction was determined not only by the experimental conditions, but also by the tendency characteristic of the given radical to stabilize itself by recombination or another method. The greater the probability of recombination (which is typical of polystyrene), the more probable was interchain exchange.

4. Hybrid polymers obtained in model systems were more polydisperse both in size and in composition. It was therefore impossible to calculate accurately the rate constants of the corresponding secondary reactions.

5. Data for systems in which a vinyl compound (styrene) was polymerized in the presence of a diene polymer (butadiene rubber) confirmed data of a series of authors on the possibility in principle of obtaining practical yields of graft polymers with a diene "backbone" and vinyl side chains by such a simple method [16].

6. The optical method of detecting hybrid polymers described may be used to establish their quantitative composition and the nephelometric titration method for a rapid qualitative detection of a hybrid polymer.

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INVESTIGATIONS IN THE FIELD OF SYNTHETIC DYES

XII. SYNTHESIS OF MONOAZO DERIVATIVES OF N-ARYLQUINALDINIUM SALTS

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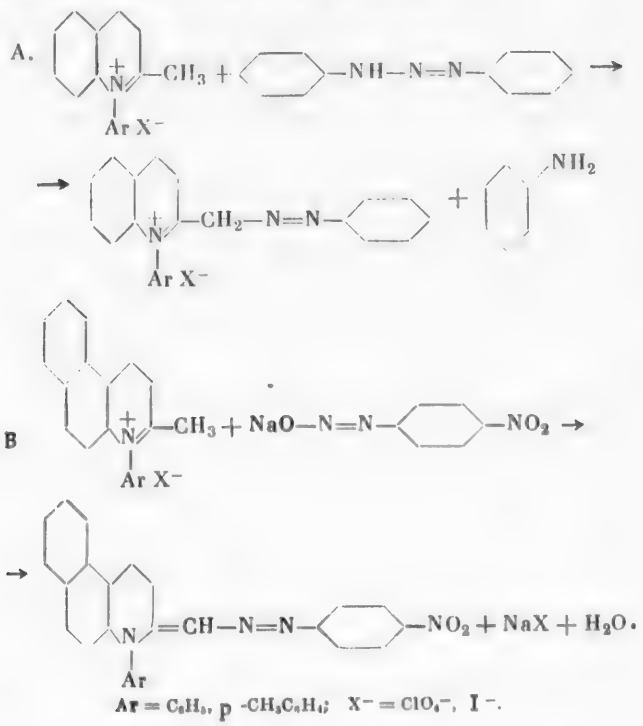
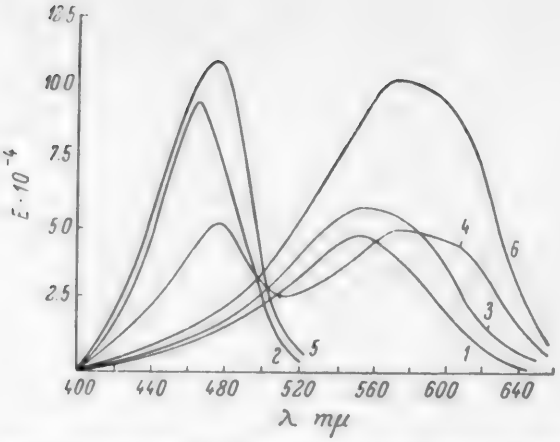
The interaction of diazonium salts with active heterocyclic bases and their quaternary salts was studied by A. E. Porai-Koshits et al. [1-5], König, Rosenhauer and others [6-8]. We showed that N-arylquinaldinium quaternary salts condense relatively readily with diazonium salts to form dyestuffs of the azo dye type [9]. In developing investigations in this direction, we studied the interaction of arylquinaldinium quaternary salts with stable forms of diazo compounds, namely, diazoaminobenzene and sodium p-nitrophenyldiazotate.

The reactions proceeded according to the following schemes:



Ar = C_6H_5, p-$CH_3C_6H_4$; $X^- = ClO_4^-$, I^-.

In the interaction of quinaldinium quaternary salts with diazoaminobenzene, the latter reacted with the elimination of the weak base, aniline, and this yielded the salt-like dye (A). In the condensations of the salts with sodium p-nitrophenyldiazotate, the methyl group was protonized with the formation of a strong base, as a result of which we obtained a dye, the base (B). During the investigations it was noticed that under our conditions, the quaternary salts did not condense with p-nitrodiazoaminobenzene. From the absorption curves it follows that



Absorption spectra. 1) 2-(p-nitrophenyldiazomethyne)-1-phenylquinoline in ethanol, 2) 2-(p-nitrophenyldiazomethyne)-1-phenylquinoline in an acid medium, 3) 2-(p-nitrophenyldiazomethyne)-1-phenylquinoline in an alkaline medium, 4) 2-(p-nitrophenyldiazomethyne)-1-phenyl-5,6-benzoquinoline in ethanol, 5) 2-(p-nitrophenyldiazomethyne)-1-phenyl-5,6-benzoquinoline in an acid medium, 6) 2-(p-nitrophenyldiazomethyne)-1-phenyl-5,6-benzoquinoline in an alkaline medium.

the monoazo dyes have a higher energy level than the analogous bisazo dyes obtained previously [9] since they absorb at longer wavelengths [10]. In comparing the spectra of the dyes obtained (see figure), it is noticed that substances containing a quinoline nucleus (A) have an absorption curve with 1 maximum, while dyes with a benzoquinoline perichrome (B) have two absorption maxima.

It is interesting that on acidification of the dye solutions, there was a strong hypsochromic shift with the blue color changing to yellow, while when the solution was made alkaline, the original color was d restored, but was deeper. Dyestuffs with a benzoquinoline structure, which had 2 maxima, had only 1 maximum with more intense absorption on being made acid or alkaline; this indicates a change in the structure and the energy state of the molecule and also the absence of excitation of vibrational levels in conjugated double bonds simultaneously with the main electronic transition [11].

EXPERIMENTAL

2-(Phenyldiazomethylene)-1-phenylquinoline perchlorate. A mixture of 0.5 g of phenylquinaldinium perchlorate, 0.31 g of diazoaminobenzene and 5 ml of ethanol was heated on a water bath for 20 minutes. Toward the end of the heating, the reaction product separated in the form of fine orange platelets with a red-violet luster. The reaction mass was left for several hours for more complete separation of the dye. We obtained 0.31 g (47%) of dye. After recrystallization from alcohol, the dye melted at 242° (with decomp.). The absorption maximum of the dye in ethanol was at 478 mμ.

Found %: Cl 8.78. $C_{22}H_{18}O_4N_3Cl$. Calculated %: Cl 8.36.

2-(Phenyldiazomethylene)-1-phenyl-5,6-benzoquinoline iodide. 0.5 g of 1-phenyl-5,6-benzoquinaldinium iodide, 0.25 g of diazoaminobenzene and 7 ml of alcohol were heated under reflux on a water bath for 30 minutes. The cooled reaction mixture deposited an orange powder. Recrystallization from alcohol gave 0.2 g (30.7%) of dye in the form of red-orange rhombic crystals with m.p. 296° (with decomp.). The absorption maximum of the dye in ethanol was at 488 mμ.

Found %: I 25.22. $C_{26}H_{20}N_2I$. Calculated %: I 25.31.

2-(Phenyldiazomethylene)-1-p-tolyl-5,6-benzoquinoline iodide. 0.5 g of 1-p-tolyl-5,6-benzoquinaldinium iodide, 0.24 g of diazoaminobenzene and 6 ml of alcohol were boiled under reflux on a water bath for 30 minutes. The reaction product began to precipitate as orange needles even during heating. The substance which had separated by next day was collected, washed with water on the filter and boiled several times with water for complete removal of the quaternary salt. Recrystallization from alcohol yielded 0.25 g (40.3%) of product. The m.p. was 300-302° (with decomp.). The absorption maximum in ethanol was at 488 mμ.

Found %: I 24.67. $C_{27}H_{22}N_2I$. Calculated %: I 24.62.

2-(p-Nitrophenyldiazomethyne)-1-phenylquinoline. 0.5 g of 1-phenylquinaldinium perchlorate was dissolved with heating in 5 ml of alcohol and to the warm solution was added a mixture of 0.29 g of sodium p-nitrophenyldiazotate and 5 ml of alcohol, after which, an intense violet color rapidly appeared. Over a period of 5-6 hours, the substance separated as a dark powder. The dye formed was collected and recrystallized from alcohol. We obtained 0.45 g (78.9%) of a substance with m.p. 218°. The absorption maximum of the substance in ethanol was at 555 mμ. The alcohol solution of the dye had a crimson-violet color and on acidification, this changed to yellow with an absorption maximum at 464 mμ and with a more intense color. Under the action of alkali the original violet-crimson color was restored, indicating the indicator properties of the dye.

Found %: N 15.18. $C_{22}H_{16}O_2N_4$. Calculated %: N 15.20.

2-(p-Nitrophenyldiazomethyne)-1-phenyl-5,6-benzoquinoline. 0.5 g of 1-phenyl-5,6-benzoquinaldinium iodide was dissolved with heating in 5 ml of alcohol, to which was added an alcohol solution of 0.24 g of sodium p-nitrophenyldiazotate in 5 ml of alcohol, when the solution immediately acquired a blue color. After 4-5 hours, the dye separated from the reaction mass as a dark blue powder. Recrystallization from pyridine yielded 0.34 g (52.8%) of a substance with m.p. 266° (with decomp.). The absorption curve had two maxima at 576 and 477 mμ; only 1 maximum remained when the solution was made acid or alkaline.

Found %: N 13.14, 13.12. $C_{26}H_{18}O_2N_4$. Calculated %: N 13.33.

2-(p-Nitrophenyldiazomethyne)-1-p-tolyl-5,6-benzoquinoline. 0.5 g of 1-p-tolyl-5,6-benzoquinaldinium iodide was dissolved with heating in 5 ml of alcohol and then a solution of 0.23 g of sodium p-nitrophenyldiazotate in 5 ml of alcohol was added to it. The whole solution became blue immediately and after some time, the reaction product separated as a dark blue powder with a metallic luster. Recrystallization from pyridine yielded 0.38 g (78.1%) of dye with m.p. 263°. The absorption curve had two maxima at 576 and 476 mμ.

Found %: N 12.68, 12.94. $C_{27}H_{20}O_2N_4$. Calculated %: N 12.95.

SUMMARY

1. It was shown that N-arylquinaldinium quaternary salts reacted chemically through the methyl group in the α-position with sodium p-nitrophenyldiazotate and diazoaminobenzene.

2. As a result of this interaction, we obtained and characterized 6 monoazo dyes, 3 in the form of salts and 3 as bases.

3. The nonsalt-like dyes with a nitro-group had indicator properties.

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N-OXIDES OF THE QUINOXALINE SERIES

III. N-OXIDES OF α-ALKYL-β-(QUINOXALYL-2)-PROPIONIC ACIDS

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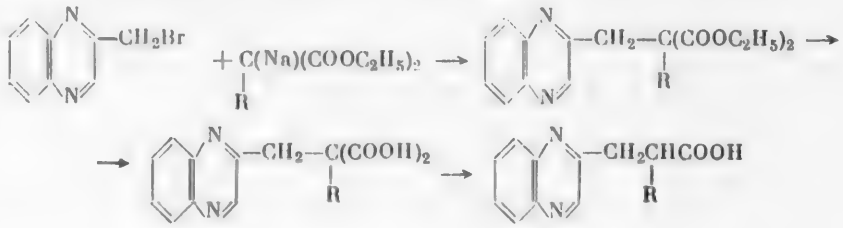
Continuing work on an investigation of the chemical and biological properties of N-oxides of the quinoxaline series [1], we undertook the synthesis of α-alkyl-β-(quinoxalyl-2)-propionic acids and their N-oxides. α-Alkyl-β-(quinoxalyl-2)-propionic acids could be obtained by the following scheme:



The starting material for this synthesis would have to be 2-bromomethylquinoxaline. Until now, all attempts to prepare 2-bromomethylquinoxaline have been unsuccessful. Bennett and Willis [2] obtained only 2-ω-tribromomethylquinoxaline in 10% yield by brominating 2-methylquinoxaline in acetic acid in the presence of sodium acetate. In 1956 Acheson confirmed these results [3] and he was also unable to stop the bromination of 2-methylquinoxaline at the formation of the monobromo derivative; attempts to reduce 2-ω-tribromomethylquinoxaline to 2-bromomethylquinoxaline were also without results. All our efforts to prepare 2-bromomethylquinoxaline by bromination of 2-methylquinoxaline in acetic acid and other organic solvents were unsuccessful; in all cases considerable tar formation was observed, especially when the reaction was carried out in nonpolar solvents. Bromination of 2-methylquinoxaline to the monobromo derivative was accomplished in a strongly acid medium (a mixture of sulfuric and acetic acids) and the yield of 2-bromomethylquinoxaline was 36.7%; 2-ω-dibromomethylquinoxaline was isolated in 26.6% yield as a second reaction product.

By condensation with the sodium derivative of malonic ester, 2-bromomethylquinoxaline was converted into the diethyl ester of [quinoxalyl-(2)-methyl]-malonic acid which was then hydrolyzed and decarboxylated; as a result, we obtained the previously known β-(quinoxalyl-2)-propionic acid [4] and thus proved the structure of the 2-bromomethylquinoxaline.

2-Bromomethylquinoxaline had a lachrimatory action; during storage, especially in light, 2-bromomethylquinoxaline darkened and gradually changed into an almost black, tarry substance, which was difficultly soluble in nonpolar organic solvents. 2-ω-Dibromomethylquinoxaline was less irritating than 2-bromomethylquinoxaline and more stable to storage, even in light.

The bromine atoms in a 2-ω-dibromomethylquinoxaline molecule did not undergo exchange reactions very readily; thus, for example, all attempts to prepare quinoxalyl-2-adehyde by heating 2-ω-dibromomethylquinoxaline with water or aqueous alcohol were unsuccessful; the bromine was replaced by hydroxyls very slowly in the presence of Na_2CO_3 or K_2CO_3. The structure of 2-ω-dibromomethylquinoxaline was established by its reaction with sodium ethylate and hydrolysis of the diethyl acetal of quinoxalyl-2-aldehyde thus formed to the previously known quinoxalyl-2-aldehyde [5]. The diethyl acetal

of quinoxalyl-2-aldehyde could not be hydrolyzed with aqueous or aqueous alcohol solution of hydrochloric acid in good yield: the reaction proceeded slowly at room temperature and strong tar formation occurred on heating. The diethyl acetal of quinoxalyl-2-aldehyde was converted into the corresponding aldehyde in relatively good yield at room temperature in a mixture of glacial acetic and hydrobromic (d 1.42) acids. A high-melting substance of unknown structure was isolated as a side product; in view of the fact that the yield of this compound increased considerably when the hydrolysis time was increased, it can be inferred that the side product formed during the hydrolysis of the diethyl acetal of quinoxalyl-2-aldehyde was the product of further conversions of quinoxalyl-2-aldehyde. The interaction of 2-bromomethylquinoxaline with the sodium derivative of diethyl ethylmalonate yielded the diethyl ester of ethyl-[quinoxalyl-(2)-methyl]-malonic acid, which was then hydrolyzed; one of the carboxyl groups of the ethyl-[quinoxalyl-(2)-methyl]-malonic acid thus formed was removed by decarboxylation to give α-ethyl-β-(quinoxalyl-2)-propionic acid. α-Isobutyl-β-(quinoxalyl-2)-propionic acid was synthesized from 2-bromomethylquinoxaline and diisobutyl isobutylmalonate by the same route. Interaction of the α-alkyl-β-(quinoxalyl-2)-propionic acids listed above with hydrogen peroxide in acetic acid yielded their di-N-oxides.

We are very grateful to O. Yu. Magidson for his interest in the present work.

EXPERIMENTAL

Bromination of 2-methylquinoxaline. 10.3 g of Br_2 in 25 ml of glacial CH_3COOH was added dropwise to a solution of 9 g of 2-methylquinoxaline in 320 ml of glacial acetic acid and 81 ml of H_2SO_4 (d 1.84), while the reaction solution was gradually heated to 70°. After addition of the bromine, the reaction solution was stirred at 70° for a further 20 minutes, cooled, poured into ice (500 g) and the precipitated 2-ω-dibromomethylquinoxaline was collected; the yield was 5 g (26.6%); after recrystallization from CH_3OH, the almost colorless crystalline substance had m.p. 120-121°.

Found %: N 9.11, 9.44; Br 52.81. $C_9H_6N_2Br_2$. Calculated %: N 9.28; Br 52.93.

To the acid mother solution remaining after separation of the 2-ω-dibromomethylquinoxaline was gradually added dry $NaHCO_3$ until pH 4 was reached. The 2-ω-bromomethylquinoxaline thus precipitated was collected, washed with water and dried in vacuum; we obtained 5.1 g (36.7%) of 2-bromomethylquinoxaline, which was purified by recrystallization from ligroine; the slightly pink crystals were readily soluble in alcohol, ether and dichloroethane and had m.p. 67-68°.

Found %: N 12.6. $C_9H_7N_2Br$. Calculated %: N 12.56.

Diethyl acetal of quinoxalyl-2-aldehyde. With stirring, 25 ml of an alcohol solution of C_2H_5ONa, prepared from 0.98 g of sodium, was gradually added to a mixture of 6.4 g of 2-ω-dibromomethylquinoxaline with 25 ml of anhydrous C_2H_5OH at 70°. The reaction mixture was stirred at 70° until the alkaline reaction (to phenolphthalein) disappeared, cooled, poured into ice water and extracted with ether. The ether solution was dried, the ether removed and the residue vacuum distilled; we obtained 3.8 g of the diethyl acetal of quinoxalyl-2-aldehyde with b.p. 124.5-125.5° (1 mm).

Found %: N 12.18; C 67.39, 67.45; H 7.1, 6.78. $C_{13}H_{16}O_2N_2$. Calculated %: N 12.06; C 67.2; H 6.9.

Hydrolysis of diethyl acetal of quinoxalyl-2-aldehyde. A solution of 1.2 g of the diethyl acetal of quinoxalyl-2-aldehyde in 5 ml of glacial CH_3COOH and 5 ml of conc. HBr (d 1.42) was left at room temperature for 30 minutes and then poured into water, neutralized to Congo with Na_2CO_3 solution and filtered; we obtained 0.2 g of a crystalline substance with m.p. 224-226° (from alcohol). The aqueous mother solution was saturated with sodium chloride and extracted with ether. The usual treatment yielded 0.5 g of quinoxalyl-2-aldehyde with m.p. 109-110° [5] (from ligroine).

The phenylhydrazone of quinoxalyl-2-aldehyde was obtained by the usual method and formed a bright yellow substance with m.p. 229-230° [5].

β-(Quinoxalyl-2)-propionic acid. To 0.11 g of finely divided metallic sodium in 10 ml of anhydrous toluene was added 0.8 g of malonic ester in 5 ml of toluene; the reaction mixture was heated until all the sodium had reacted. 1.1 g of 2-bromomethylquinoxaline was gradually added with stirring at 20-25° to the solution obtained, after which the temperature was raised to the boiling point and the reaction mixture stirred until the alkaline reaction (to phenolphthalein) disappeared. At the end of the reaction, the toluene was removed in vacuum and the

residue treated with water and extracted with ether. The ether extract was dried and the ether removed; to the residue (1.05 g) was added 5 ml of 15% NaOH solution and the reaction mixture boiled until all the solid dissolved; the solution obtained was stirred with activated charcoal and filtered and the filtrate acidified to pH 4 and saturated with $(NH_4)_2SO_4$ to liberate [quinoxalyl-(2)-methyl]-malonic acid with m.p. 95-96° (from water). The [quinoxalyl-(2)-methyl]-malonic acid obtained was heated at its melting point until the evolution of CO_2 ceased, then the melt dissolved in aqueous $NaHCO_3$ solution and the solution purified with activated charcoal, filtered, acidified to pH 4 and saturated with sodium chloride. The precipitate was extracted with benzene. Evaporation of benzene left β-(quinoxalyl-2)-propionic acid (0.55 g) with m.p. 115-116°; a mixed melting point with β-(quinoxalyl-2)-propionic acid obtained by the usual method [4] was not depressed.

α-Ethyl-β-(quinoxalyl-2)-propionic acid. a) Ethyl-[quinoxalyl-(2)-methyl]-malonic acid. To 0.36 g of finely divided sodium in 15 ml of anhydrous toluene was added 3.3 g of diethyl ethylmalonate in 5 ml of anhydrous toluene. The reaction mixture was boiled until all the sodium had reacted, then to the cooled solution was added 3.3 g of 2-bromomethylquinoxaline in 5 ml of toluene and the reaction mixture boiled and stirred for 3 hours, cooled, poured into ice-water and the toluene layer separated; removal of the toluene left 4.30 g of an oily substance. The substance obtained was dissolved in 15 ml of a 10% alcohol solution of KOH and boiled for 1.5 hours. The solution was cooled and the crystalline sodium salt of ethyl-[quinoxalyl-(2)-methyl]-malonic acid collected, dissolved in water and acidified to liberate ethyl-[quinoxalyl-(2)-methyl]-malonic acid in a yield of 2.1 g (50.6%) and having m.p. 144-145° (from aqueous alcohol).

Found %: N 10.00; C 61.11, 61.36; H 5.36, 5.18. $C_{14}H_{14}O_4N_2$. Calculated %: N 10.22; C 61.28; H 5.14.

b) Decarboxylation of ethyl-[quinoxalyl-(2)-methyl]-malonic acid. 1 g of ethyl-[quinoxalyl-(2)-methyl]-malonic acid was heated at 145° until the evolution of CO_2 ceased. The melt obtained was dissolved in sodium carbonate solution and extracted with ether. The aqueous alkaline layer was treated with activated charcoal and filtered; the filtrate was made slightly acid to Congo with dilute HCl solution and extracted with ether. The ether extract was washed with water and dried with anhydrous Na_2SO_4. Removal of the ether yielded 0.8 g of α-ethyl-β-(quinoxalyl-2)-propionic acid, which was isolated in the form of an oily substance that slowly crystallized on standing in a cold place; the colorless crystals had m.p. 69-70° [from ligroine (80-120°)].

Found %: N 12.37. $C_{13}H_{14}O_2N_2$. Calculated %: N 12.17.

α-Isobutyl-β-(quinoxalyl-2)-propionic acid. To 0.31 g of finely divided metallic Na in 20 ml of anhydrous toluene was added a solution of 4.62 g of the isobutyl ester of isobutylmalonic acid in 10 ml of toluene. The reaction mixture was heated until all the sodium had reacted and then a solution of 3.28 g of 2-bromomethylquinoxaline in 10 ml of toluene was gradually added with stirring (temperature 65-70°). After the addition of the 2-bromomethylquinoxaline, the reaction mixture was boiled with stirring for 3 hours until the alkaline reaction to phenolphthalein disappeared, cooled and poured into water. The toluene layer was separated, washed with water and dried and the toluene removed in vacuum. To the 5.76 g of oily substance obtained after removal of the toluene was added 21 ml of a 10% alcohol solution of KOH and the reaction mixture boiled for 2 hours, after which the alcohol was removed and the residue dissolved in water; the aqueous alkaline solution was extracted with ether, treated with activated charcoal, filtered and made weakly acid to Congo and the caramel-like substance thus liberated was extracted with ether. The substance obtained after removal of the ether was heated at 125° and then at 133° until the evolution of CO_2 ceased and dissolved in ether and the ether solution extracted with aqueous Na_2CO_3 solution. The aqueous alkaline solution was treated with activated charcoal, filtered, acidified to pH 3 and extracted with ether. Removal of the ether yielded 2.5 g of α-isobutyl-β-(quinoxalyl-2)-propionic acid: the oily substance crystallized on standing and had m.p. 104-105° (from a mixture of ligroine and acetone).

Found %: N 10.89; C 69.73; H 6.91. $C_{15}H_{18}O_2N_2$. Calculated %: N 10.85; C 69.72; H 7.03.

1,4-Di-N-oxide of α-ethyl-β-(quinoxalyl-2)-propionic acid. A mixture of 8 ml of glacial CH_3COOH, 1.4 ml of acetic anhydride and 2 ml of 40% H_2O_2 was left for 12 hours (during this time the temperature rose spontaneously to 30-40° and then fell to room temperature) and then 0.4 g of α-ethyl-β-(quinoxalyl-2)-propionic acid was added and the mixture heated at 50° for 16 hours. The reaction solution was evaporated to small volume in vacuum at a temperature of not more than 40-45°, ether added until turbidity appeared and the mixture cooled; we obtained the 1,4-di-N-oxide of α-ethyl-β-(quinoxalyl-2)-propionic acid (0.3 g) as a light yellow crystalline substance with m.p. 176-177° (decomp.) (from C_2H_5OH).

Found %: N 10.9. $C_{13}H_{14}O_4N_2$. Calculated %: N 10.7.

1,4-Di-N-oxide of α-isobutyl-β-(quinoxalyl-2)-propionic acid. By a method analogous to the one described above, from 2.28 of α-isobutyl-β-(quinoxalyl-2)-propionic acid, 15.5 ml of 30% H_2O_2 solution, 62 ml of glacial CH_3COOH and 11 ml of acetic anhydride we obtained 1.7 g of the 1,4-di-N-oxide of α-isobutyl-β-(quinoxalyl-2)-propionic acid; the light yellow crystalline substance had m.p. 175-176° (from C_2H_5OH).

Found %: N 9.41, 9.95; C 61.86, 62.39; H 6.42, 6.55. $C_{15}H_{18}O_4N_2$. Calculated %: N 9.65; C 62.05; H 6.25.

SUMMARY

1. It was established that the bromination of 2-methylquinoxaline with bromine in a mixture of acetic and concentrated sulfuric acids formed 36.7% of 2-ω-bromomethylquinoxaline and 26.6% of 2-ω-dibromomethylquinoxaline.

2. Condensation of 2-bromomethylquinoxaline with the sodium derivatives of alkylmalonic esters with subsequent hydrolysis of the condensation products and removal of one of the carboxyl groups by decarboxylation yielded α-alkyl-β-(quinoxalyl-2)-propionic acids.

3. Oxidation of the α-alkyl-β-(quinoxalyl-2)-propionic acids with Perhydrol in CH_3COOH gave the 1,4-di-N-oxides of α-alkyl-β-(quinoxalyl-2)-propionic acids.

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HYDROXYMETHYLENE KETONES

II. PREPARATION OF ALKOXYMETHYLENECYCLOHEXANONES AND THEIR CONVERSIONS IN REDUCTION REACTIONS [1]

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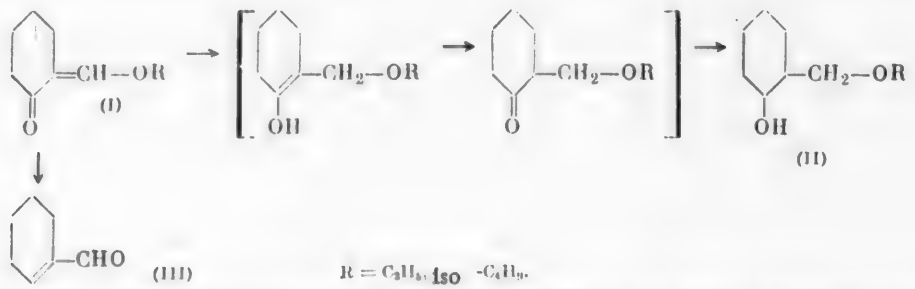
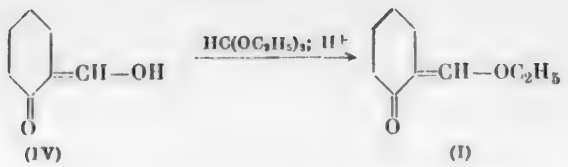
The formation of unsaturated aldehydes in a mixture with 1,3-glycols by the reduction of enolizable β - dicarbonyl compounds with lithium hydride was described by Dreiding and Hartman [2]. In the opinion of these authors, reduction of the "normal" forms led to diols and the enolized part reacted with lithium aluminum hydride to form enolate salts, which underwent further attack by the hydride at one of the carbonyl groups and were converted into simple enolates, incapable of further reduction. The intermediate compounds formed lost the elements of a water molecule and were converted into α,β -unsaturated carbonyl compounds.

We were convinced that alkoxymethylene-β -carbonyl compounds behave in the same way (cf. also [3]). Thus, when reduced with lithium aluminum hydride at 20°, the isobutyl ester of α-formylcyclohexanone (I, R = = iso-C_4H_9) gave a 70% yield of tetrahydrobenzaldehyde (III). When reduced with aluminum isopropoxide in isopropyl alcohol at 95°, (I) was also converted into tetrahydrobenzaldehyde, which was isolated in 24-25% yield. Reduction with nascent hydrogen tended to saturate all the multiple bonds. Thus, for example, in the reduction of alkoxymethylene-β -carbonyl compounds (I) with sodium in moist ether, the reaction tended toward the 1,4-addition of the first hydrogen molecule and ended with the formation of the hydroxy ether (II).



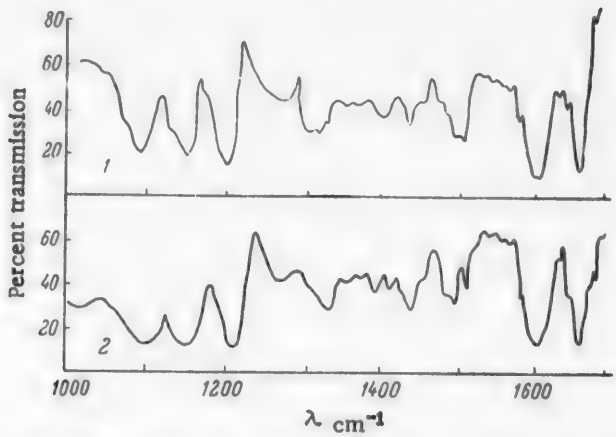
The hydroxy ether (II) was not hydrolyzed by dilute mineral acids and formed derivatives through the hydroxyl group.

Following the directions of Ruzicka et al. [4], we attempted to prepare acetals of formylcyclohexanone by treating the latter with orthoformic ester in the presence of concentrated hydrochloric acid, for their subsequent reduction to hydroxy acetals. Like Royals and Brannock [6], despite careful repetition of the conditions, we were unable to repeat the results of the Swiss investigators. Under the conditions of these authors and when the concentrated hydrochloric acid was replaced by orthophosphoric, with the addition of p-toluenesulfonic acid to the latter and also in experiments with ammonium nitrate, the ethyl ether of α-hydroxymethylenecyclohexanone (I, R = C_2H_5) was formed in various yields.



(IV) (I)

The IR absorption spectrum of the ethoxymethylenecyclohexanone formed (I, R = C_2H_5) coincided in the position of the valence oscillation of the C =O group, reduced by conjugation (1685 cm^{-1}), and likewise for the frequency of the conjugated −C=C− bond (1600 cm^{-1}) and the ether bond =C−O− (1250 cm^{-1}) with the spectrum of the corresponding isobutyl derivative (I, R = iso-C_4H_9) (see figure).



IR absorption spectra. 1) Isobutoxymethylenecyclohexanone (I, R = = iso-C_4H_9), 2) ethoxymethylenecyclohexanone (I, R = C_2H_5).

The reduction of ethoxymethylenecyclohexanone with lithium aluminum hydride and sodium in moist ether proceeded exactly as described above for the isobutyl ether of α-formylcyclohexanone. Thus, enolizable β-dicarbonyl compounds behave anomalously in the reaction with orthoformic ester and form ethyl ethers of the enol forms instead of acetals.

The authors would like to thank N. A. Preobrazhenskii and G. I. Samokhvalov for participating in the discussion of the results and L. V. Luk'yanova for plotting and interpreting the IR spectra.

EXPERIMENTAL

1. α-Formylcyclohexanone was obtained according to [6] in 73% yield. The semicarbazone had m.p. 177-178° (from alcohol).

Found %: N 23.10, 22.95. $H_{13}O_2N_3$. Calculated %: N 22.92.

2. The isobutyl ether of α-hydroxymethylenecyclohexanone (I, R = iso-C_4H_9) was obtained according to [7] in 84% yield and had $n^{24}D$ 1.4865 ($n^{25}D$ 1.4865 [7]).

I. Reduction of isobutyl ether of α-hydroxymethylenecyclohexanone (I, R = iso-C_4H_9).

a) Action of lithium aluminum hydride. Over a period of 40 minutes, 7.0 g of the isobutyl ether of α-hydroxymethylenecyclohexanone in 7 ml of anhydrous ether was added to a solution of lithium aluminum hydride in dry ether (30 ml containing 0.042 g of lithium aluminum hydride per ml of solution), cooled to −50°. After 2 hours the temperature of the reaction mass was raised to 20° and the mixture was left for 12 hours; 40 g of ice was then added and the mixture extracted with ether. The ether extract was dried with magnesium sulfate, the ether evaporated and the residue distilled under reduced pressure. We obtained 2.9 g (70%) of tetrahydrobenzaldehyde with b.p. 56-58° at 9 mm and $n^{21}D$ 1.4880 ($n^{19}D$ 1.4914 [7]).

Found %: C 76.10, 75.83; H 8.60, 8.87. $C_7H_{10}O$. Calculated %: C 76.36; H 9.09.

The 2,4-dinitrophenylhydrazone had m.p. 212-213° (from alcohol) (212-212.5° [7]). The semicarbazone had m.p. 208-209° (from alcohol). The material of the 1st fraction with b.p. 30-32° at 9 mm was isobutyl alcohol and its α-naphthylurethan had m.p. 98-99° (from ligroine with b.p. 100-130°).

Found %: C 74.43, 74.66; H 7.05, 6.76. $C_{15}H_{17}O_2N$. Calculated %: C 74.07; H 6.99.

b) Action of aluminum isopropoxide. 15.0 g (0.82 mole) of the isobutyl ether of α-hydroxymethylenecyclohexanone was added to a solution of 18.0 g (0.88 mole) of distilled aluminum isopropoxide in 80 ml of anhydrous isopropyl alcohol and the mixture heated at 95° for 5 hours. The reaction mass was cooled, decomposed with 80 ml of 10% sodium hydroxide solution and exhaustively extracted with ether. The extract was dried with magnesium sulfate, the ether removed and the residue distilled under reduced pressure. We obtained 2.2 g (24.2%) of tetrahydrobenzaldehyde with b.p. 80-82° at 21 mm. The 2,4-dinitrophenylhydrazone had m.p. 211-212° (from alcohol). The semicarbazone had m.p. 208.5-209.5° (from alcohol). Mixed melting points of these derivatives with the corresponding derivatives of tetrahydrobenzaldehyde obtained in Experiment a were not depressed.

Analysis of semicarbazone. Found %: N 25.42, 25.31. $C_8H_{13}O_2N_3$. Calculated %: N 25.15.

c) Action of sodium in moist ether. With vigorous stirring, 9.0 g (0.83 mole) of sodium was added in small portions to 23.0 g (0.126 mole) of the isobutyl ether of α-hydroxymethylenecyclohexanone in 125 ml of ether and 70 ml of water at −10°. The addition of the sodium required about 10 hours. The aqueous layer was separated and the ether layer washed with water to a neutral reaction (to litmus). The ether extracts were dried with magnesium sulfate, the solvent evaporated and the residue distilled under reduced pressure. We obtained 9.2 g (40%) of the isobutyl ether of α-hydroxymethylcyclohexanol (II, R = iso-C_4H_9) with b.p. 118-122° (13 mm), $n^{25}D$ 1.4547, d^{25}_4 0.9327, MR_D 53.57; calc. 53.41.

Found %: C 70.70, 70.45; H 11.72, 11.79. $C_{11}H_{22}O_2$. Calculated %: C 70.90; H 11.80.

The 3,5-dinitrobenzoate had m.p. 57-59°.

Found %: N 7.62. $C_{18}H_{24}O_7N_2$. Calculated %: N 7.36.

Attempts to hydrolyze the isobutyl ether of α-hydroxymethylcyclohexanol (II) [10] led to the following results. 3.0 g (0.016 mole) of (II) was mixed at 0° with 60 ml of anhydrous alcohol containing 3 ml of 20% sulfuric acid. The reaction mass was left for 12 hours at 20° and then part of the alcohol was evaporated under reduced pressure. The residue was poured into 200 ml of water and extracted with ether. The ether extract was dried with magnesium sulfate, the solvent evaporated and the residue evaporated at reduced pressure. We obtained 2.3 g of the starting compound (II, R = iso-C_4H_9) with b.p. 120-122° (14.5 mm), $n^{18.5}D$ 1.4552, $d^{18.5}_4$ 0.9321, MR_D 53.39; calc. 53.41.

Found %: C 70.73, 70.45; H 11.53, 11.68. $C_{11}H_{22}O_2$. Calculated %: C 70.90; H 11.80.

II. Interaction of α-hydroxymethylenecyclohexanone (IV) with ethyl orthoformate. a) In the presence of orthoformic acid and traces of p-toluenesulfonic acid [8]. To a mixture of 15.7 g (0.125 mole) of α-formylcyclohexanone and 19.6 g (0.156 mole) of ethyl orthoformate was added a solution of 0.4 ml of 85% orthophosphoric acid in 4 ml of anhydrous alcohol, containing traces of p-toluenesulfonic acid. The reaction mass was left for 12-14 hours, during which time, the solution changed color from dark green to dark crimson. Ether (40 ml) was added and the mixture washed with 5% sodium hydroxide solution and water. The ether layer was dried with magnesium sulfate, the solvent evaporated and the residue distilled under reduced pressure. We obtained 13.7 g (71.4%) of the ethyl ether of α-hydroxymethylenecyclohexanone (I, R = C_2H_5).

B.p. 82-89° (1 mm), $n^{22}D$ 1.5028, d^{22}_4 1.029, MR_D 44.18; calc. 43.80.
Found %: C 69.82, 69.87; H 9.17, 9.13. $C_9H_{14}O_2$. Calculated %: C 70.06; H 9.11.

The product gave a crimson color with an aqueous alcohol solution of ferric chloride on standing. The semicarbazone had m.p. 182-183° (from alcohol).

Found %: C 58.32, 58.29; H 6.80, 6.69; N 25.70, 25.66. $C_8H_{11}ON_3$. Calculated %: C 58.11; H 6.71; N 25.43.

b) In the presence of orthophosphoric acid. 4.15 g (0.033 mole) of α-formylcyclohexanone was mixed with 6.94 g (0.07 mole) of ethyl orthoformate. The mixture was heated to 40°, a solution of 0.2 g of orthophosphoric acid in 2 ml of anhydrous alcohol added and the reaction mixture left for 20 hours. Subsequent processing was as in Experiment a. We obtained 3.02 g (59.6%) of the ethyl ether of α-hydroxymethylenecyclohexanone.

B.p. 106-112° (10 mm), $n^{17}D$ 1.5050, d^{17}_4 1.032, MR_D 44.26; calc. 43.80.

c) In the presence of concentrated hydrochloric acid [4]. To a mixture of 3.8 g (0.03 mole) of α-formylcyclohexanone and 4.88 g (0.05 mole) of ethyl orthoformate in 4.5 ml of anhydrous alcohol was added 1 drop of concentrated hydrochloric acid and the mixture left for 12 hours. Subsequent processing of the reaction mass was as in Experiment a. We obtained 0.68 g (14.8%) of the ethyl ether of α-hydroxymethylenecyclohexanone.

B.p. 118-123° (15 mm), $n^{20}D$ 1.4995, d^{20}_4 1.025, MR_D 44.10; calc. 43.80.

d) In the presence of ammonium nitrate [9]. To a mixture of 7.3 g (0.058 mole) of α-hydroxymethylenecyclohexanone and 12.8 g (0.131 mole) of ethyl orthoformate was added a solution of 0.24 g of ammonium nitrate in 4.3 ml of anhydrous alcohol, which was heated to 50°. After 24 hours the reaction mass was treated as described in Experiment a. We obtained 3.2 g (35.9%) of the ethyl ether of α-hydroxymethylenecyclohexanone.

B.p. 122-126° (18 mm), $n^{20}D$ 1.4828, d^{20}_4 0.9986, MR_D 44.13; calc. 43.80.

The ethyl ether of α-hydroxymethylenecyclohexanone was also obtained by the interaction of α-hydroxymethylenecyclohexanone with a 5-fold amount of alcohol and concentrated hydrochloric acid in a yield of 50.7%.

III. Reduction of α-ethoxymethylenecyclohexanone (I, R = C_2H_5). a) Action of lithium aluminum hydride. The reaction was carried out as described in section I, a. From 7.7 g of α-methoxymethylenecyclohexanone (I) we obtained 2.67 g (55%) of tetrahydrobenzaldehyde.

B.p. 55-58° (8 mm), $n^{22}D$ 1.4880, d^{22}_4 0.9821, MR_D 32.27; calc. 31.87.

The semicarbazone had m.p. 208.5-209° (from alcohol).

Found %: N 25.12, 24.84. $C_8H_{13}ON_3$. Calculated %: N 25.14.

The 2,4-dinitrophenylhydrazone had m.p. 212-213° (from alcohol).

Found %: C 53.92, 54.08; H 4.86, 4.95. $C_{13}H_{14}O_4N_4$. Calculated %: C 53.78; H 4.86.

b) Action of sodium in moist ether. The reaction was carried out under the conditions described in section I, c. From 12.5 g of α-ethoxymethylenecyclohexanone (I, R = C_2H_5) we obtained 4.22 g (33%) of α-ethoxymethylcyclohexanol (II, R = C_2H_5).

B.p. 90-96° (8 mm), $n^{24}D$ 1.4559, d^{24}_4 0.9615, MR_D 44.82; calc. 44.61.

Found %: C 68.35, 67.92; H 11.58, 11.47; $H_{act.}$ 0.684, 0.665. $C_9H_{18}O_2$. Calculated %: C 68.31; H 11.47; $H_{act.}$ 0.632.

SUMMARY

1. It was shown that the reduction of alkoxymethylenecyclohexanones with lithium aluminum hydride and aluminum isopropoxide led to α, β-unsaturated tetrahydrobenzaldehyde and that 2 molecules of hydrogen were added by the action of sodium in moist ether to form hydroxy ethers.

2. The interaction of α-formylcyclohexanone with orthoformic ester under the action of acid catalysts formed ethoxymethylene cyclohexanone instead of keto acetals.

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INVESTIGATIONS IN THE FIELD OF QUINONES

XXVII. SYNTHESIS OF ARYLNAPHTHOQUINONES AND THEIR REACTION WITH SODIUM CYANIDE

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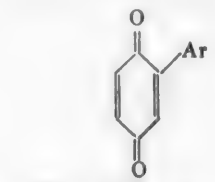
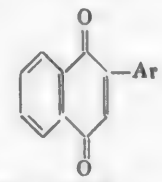
The problem of the effect of the electron donor-acceptor properties of substituents in the quinone nucleus on reactivity, the type of process and the direction of orientation is still unsolved. This work is difficult as reactions in the quinone series are accompanied, as a rule, by the side reactions of quinone polymerization, isomerization and cleavage of intermediate compounds and, finally, oxidation-reduction processes. In addition, considerable difficulties are caused by the absence of preparative methods for obtaining substituted p-quinones.

In the present work we synthesized 2-aryl-1,4-naphthoquinones (V)-(VIII) from aryl-1,4-benzoquinones (I)-(IV) and butadiene by a procedure developed previously on other examples [1].



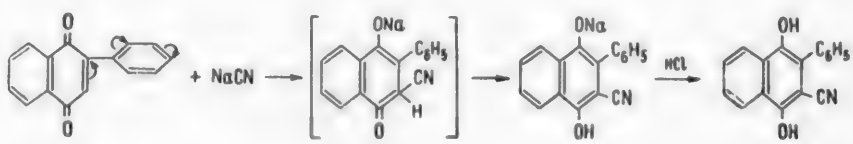
(I) Ar = C_6H_5
(II) Ar = $C_6H_4CH_3$-p
(III) Ar = $C_6H_4OCH_3$-p
(IV) Ar = $C_6H_4NO_2$-p



(V) Ar = C_6H_5
(VI) Ar = $C_6H_4CH_3$-p
(VII) Ar = $C_6H_4OCH_3$-p
(VIII) Ar = $C_6H_4NO_2$-p

Aryl-1,4-benzoquinones (I)-(IV) were synthesized in high yields by simply arylating p-benzoquinone with diazo compounds by a procedure which differed from that described in the German patent [2] in that sodium acetate was added to the quinone solution several minutes before the diazo compound.

We considered that the effect of the aryl substituent could facilitate nucleophilic addition. The reaction of 2-aryl-1,4-naphthoquinones with sodium cyanide was studied as an example of nucleophilic addition.



2-Aryl-1,4-naphthoquinones were reacted with sodium cyanide by gradual addition of a solution of quinone in dioxane to an aqueous alcohol solution of sodium cyanide in an atmosphere of nitrogen. Sodium cyanide added especially readily to 2-(p-nitrophenyl)-1,4-naphthoquinone (VIII). The reaction with other 2-aryl-1,4-naphthoquinones was accompanied by the formation of a small amount of tars. Cyanohydroquinones could not be isolated in the reaction of p-benzoquinone, 1,4-naphthoquinone and 2-methyl-1,4-naphthoquinone with

sodium cyanide. The structure of the 2-aryl-3-cyanonaphthohydroquinones obtained was confirmed by their oxidation to the corresponding quinones, by analysis data and by qualitative reactions.

(IX) Ar = C_6H_5
(X) Ar = $C_6H_4CH_3$-p
(XI) Ar = $C_6H_4OCH_3$-p
(XII) Ar = $C_6H_4NO_2$-p

(XIII) Ar = C_6H_5
(XIV) Ar = $C_6H_4CH_3$-p
(XV) Ar = $C_6H_4OCH_3$-p
(XVI) Ar = $C_6H_4NO_2$-p

The benzoyl (XVII) and methyl (XVIII) and (XIX) derivatives were prepared for 2-phenyl-3-cyanonaphthohydroquinone (IX).

EXPERIMENTAL

Phenyl-1,4-benzoquinone (I). 9.3 g (0.1 mole) of aniline was diazotized by the usual method. The solution of the diazonium salt was immediately added with vigorous stirring to a solution of 11 g (0.1 mole) of p-benzoquinone in 120 ml of alcohol and 600 ml of distilled water,* mixed with a solution of 25-30 g (0.23-0.27 mole) of crystalline sodium acetate in 100 ml of water a few minutes before the addition of the diazo salt solution. The temperature of the reaction solution was 18-20° and the pH 5-5.5. The evolution of nitrogen and formation of a precipitate of (I) began immediately. After 30-40 minutes, the precipitate was collected by filtration. Crystals of (I) again separated from the filtrate after 30-40 minutes. These were also collected. The yield of (I) with m.p. 109-111° was 14.4 g (80%). After recrystallization from alcohol, the substance had m.p. 112.5-113.5°. According to literature data, the m.p. is 114° [3].

The other aryl-1,4-benzoquinones were synthesized analogously. The yields and melting points are given in Table 1.

TABLE 1

Aryl-1,4-benzoquinones

Name of compound	Yield (in %)	Melting point	
		found	according to literature data
p-Tolyl-1,4-benzoquinone (II)	83.5	138-139° (from alcohol)	138-139° [3]
p-Anisyl-1,4-benzoquinone (III)	82	112-113 (from alcohol)	112-113 [5], 120-121 [3]
p-Nitrophenyl-1,4-benzoquinone (IV)	70	129-130	135 [6]

2-Phenyl-1,4-naphthoquinone (V). While cooled in ice, 90 ml of acetic acid was saturated with 23 g (0.43 mole) of butadiene. To the solution obtained was added 36.8 g (0.2 mole) of (I). The reaction mixture was left for 2 days in a closed vessel and shaken from time to time. To isomerize the adduct formed, we then boiled the mixture for 2 hours and diluted it two-fold with acetic acid. To the solution obtained was gradually added a solution of chromic acid (54 g of chromium trioxide in 52 ml of water) in such a way that the temperature did not rise above 75°. When all the oxidant had been added, the reaction solution was heated for 1 hour at 70-75°, cooled to room temperature and diluted with 1.5-2 volumes of water. The crystals of (V) were collected and dried in a vacuum desiccator over calcium chloride. The yield of (V) with m.p. 104-108° was 38.3 g (82%). After recrystallization from alcohol, the product had m.p. 111-112°. According to literature data the m.p. is 112-113° [4] and 110° [3].

The yields and melting points of the other 2-aryl-1,4-naphthoquinones obtained analogously are presented in Table 2.

*The quinone was dissolved in alcohol by heating and when the solution had cooled to room temperature, it was poured into water. If a precipitate of quinone appeared at this point, then the aqueous alcohol solution was heated until the precipitate dissolved and then cooled to room temperature.

TABLE 2

2-Aryl-1,4-naphthoquinones

Name of compound	Yield (in %)	Melting point		Analysis data (in %)			
				found		calc.	
		found	according to literature data	C	H	C	H
2-(p-Tolyl)-1,4-naphthoquinone (VI)	52	110.5—111° (from alcohol)	--	82.08, 82.08	4.88, 4.93	82.24	4.87
2-(p-Anisyl)-1,4-naphthoquinone (VII)	91	122—123 (from ligroine)	--	77.08, 77.12	4.70, 4.67	77.24	4.58
2-(p-Nitrophenyl)-1,4-naphthoquinone (VIII)	72	218—219 (from alcohol)	223—224° [7]				

2-Phenyl-3-cyanonaphthohydroquinone (IX). A solution of 4.7 g (0.02 mole) of (V) in 30 ml of dioxane was added over 15-20 minutes with vigorous stirring to a solution of 3 g (0.06 mole) of sodium cyanide in 15 ml of water and 15 ml of alcohol. The reaction was carried out at room temperature in an atmosphere of nitrogen. The dark red solution obtained was acidified with 30 ml of 2 N hydrochloric acid, diluted with water. The brownish oil thus liberated solidified on cooling and the crystals obtained were collected. Over a period of 2-3 hours, the mother solution deposited more precipitate, The crystal were washed with water, dried and washed free from tarry impurities with benzene. The yield of (IX) was 4 g (78%) and the m.p. was 184° (from benzene). The substance was readily soluble in alcohol, dioxane, dichloroethane and acetone and difficultly so in benzene.

Found %: C 78.10, 78.00; H 4.29, 4.28. $C_{17}H_{11}O_2N$. Calculated %: C 78.12; H 4.24.

The yields and melting points of the other 2-aryl-3-cyanonaphthohydroquinones, which were obtained analogously, are given in Table 3.

2-Phenyl-3-cyano-1,4-naphthoquinone (XIII). A solution of 2 g of ferric chloride in 20 ml of water was gradually added with stirring to a solution of 1 g (0.0038 mole) of (IX) in 20 ml of alcohol. The suspension obtained was diluted two-fold with water. The precipitate was collected, washed with water and alcohol and dried. The yield of (XIII) was 0.8 g (80%) and the m.p. 176-177°. The substance was readily soluble in acetic acid, benzene and acetone and difficultly soluble in alcohol and ligroine.

Found %: C 78.39, 78.38; H 3.58, 3.77. $C_{17}H_9O_2N$. Calculated %: C 78.75; H 3.50.

TABLE 3

2-Aryl-3-cyanonaphthohydroquinones

Name of compound	Yield (in %)	Melting point	Analysis data (in %)			
			found		calc.	
			C	H	C	H
2-(p-Tolyl)-3-cyanonaphthohydroquinone (X)	84	169—170° (from alcohol)	78.40, 78.34	4.87, 4.89	78.53	4.76
2-(p-Anisyl)-3-cyanonaphthohydroquinone (XI)	64	238.5—240 (from benzene)	74.46, 74.27	4.62, 4.34	74.21	4.50
2-(p-Nitrophenyl)-3-cyanonaphthohydroquinone (XII)	82	233—234 (from chloroform)	66.83, 66.64	3.47, 3.46	66.66	3.29

TABLE 4

2-Aryl-3-cyano-1,4-naphthoquinones

Name of compound	Yield (in %)	Melting point	Analysis data (in %)			
			found		calc.	
			C	H	C	H
2-(p-Tolyl)3-cyano-1,4--naphthoquinone (XIV)	70	176—177° (from alcohol)	79.34, 79.15	4.16, 4.19	79.11	4.06
2-(p-Anisyl)-3-cyano-1,4-naphthoquinone (XV)	83	172—173 (from alcohol)	74.87, 74.79	3.94, 3.92	74.73	3.83
2-(p-Nitrophenyl)-3-cyano-1,4-naphthoquinone (XVI)	70	185—186 (from acetic acid)	66.83, 66.98	2.63, 2.73	67.11	2.65

The yields and melting points of the other 2-aryl-3-cyano-1,4-naphthoquinones obtained analogously are given in Table 4.

Methylation of 2-phenyl-3-cyanonaphthohydroquinone (IX). A solution of 4.2 g of (IX) was mixed with 32 ml of 2 N sodium hydroxide and 6.4 ml of dimethyl sulfate. The reaction mixture was shaken in a closed bottle for 45 minutes. Dilution with water produced a precipitate (3.2 g) with m.p. 137-140°. After three recrystallizations from alcohol, the product had m.p. 145-145.5°. A test for nitrogen was positive.

Found %: C 78.75, 78.74; H 5.29, 5.31. $C_{19}H_{15}O_2N$. Calculated %: C 78.87; H 5.23.

The substance was insoluble in alkali and gave no color with ferric chloride; it was readily soluble in ether, benzene and dichloroethane. According to analysis data and properties, the substance obtained was the dimethyl ether of 2-phenyl-3-cyanonaphthohydroquinone (XVIII).

The mother solution obtained after the first recrystallization of the substance described above was diluted with water (1/5 of its volume) to precipitate crystals of the monomethyl ether of 2-phenyl-3-cyanonaphthohydroquinone (XIX) with m.p. 174-188°. Recrystallization from cyclohexane yielded fluffy white crystals with m.p. 210-211°. A test for nitrogen was positive. The substance was soluble in alkali solution and gave a blue color with ferric chloride in the presence of pyridine.

Found %: C 78.65; H 4.95. $C_{18}H_{13}O_2N$. Calculated %: C 78.75; H 4.77.

Dibenzoyl-2-phenyl-3-cyanonaphthohydroquinone (XVII). A mixture of 1.3 g of (IX) and 1.2 g of benzoyl chloride was heated for 1 hour at 100°. The temperature was then raised to 125° and the mixture heated until the evolution of hydrogen chloride ceased. The substance (XVII) obtained was washed with ether. The yield was 1 g (42%) and the m.p. 240-241° [from a mixture of alcohol and acetone (1:1)].

Substance (XVII) was difficultly soluble in alcohol, ether, acetic acid and cyclohexanone and readily soluble in dioxane, acetone, chloroform and benzene.

Found %: C 79.17, 79.22; H 4.14, 4.10. $C_{31}H_{19}O_4N$. Calculated %: C 79.30; H 4.05.

SUMMARY

1. It was shown that in the arylation of p-benzoquinone with diazo compounds, preliminary activation of the former with sodium acetate accelerated the process and increased the yield of arylbenzoquinones. The arylbenzoquinones and butadiene gave 2-aryl-1,4-naphthoquinones.

2. Sodium cyanide was added to quinones for the first time using 2-aryl-1,4-naphthoquinones as the example. It was established that the reaction gave 2-aryl-3-cyano-1,4-naphthohydroquinones.

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INVESTIGATIONS IN THE FIELD OF QUINONES

XXVIII. SYNTHESIS OF 5-HYDROXYINDOLE DERIVATIVES

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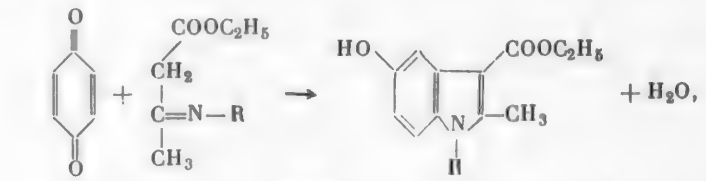
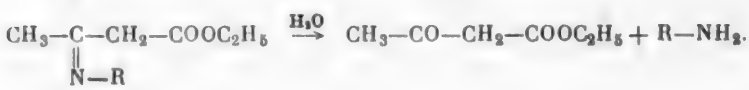
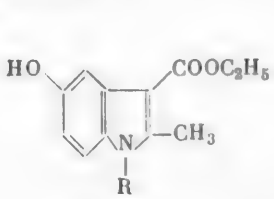
We showed in our work [1-5] that condensation of p-quinones with β-aminocrotonic ester and its analogs was a reliable method of synthesizing 5-hydroxyindole derivatives, but in a number of cases the yield of the latter was quite small. In one of our works [4] we used a procedure, namely, mixing the reagents with strong cooling and then rapid heating of the reaction mixture, which gave a 70% yield of the 5-hydroxyindole derivative in the condensation of N-ethyl-β-aminocrotonic ester with p-benzoquinone. However, this procedure was not suitable for increasing the yield of other 5-hydroxyindole derivatives.

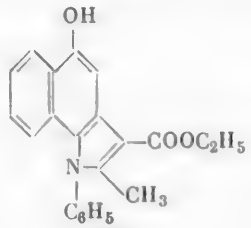
In connection with the interest in the synthesis of serotonin analogs [6] and of plant growth stimulants [7, 8] based on 5-hydroxyindole derivatives, we again attempted to increase the yield of indole derivatives. We based our development of the reaction conditions on the hypothesis that the water formed during condensation hydrolyzed the β-aminocrotonic ester.



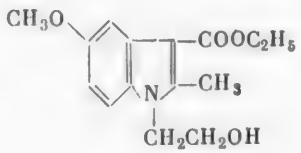


Liberation of ammonia and amines caused polymerization of the starting quinone and other side reactions. We wished to use acetic anhydride and zinc chloride for binding the water, but obtained a negative result. The indole yield did not rise in the presence of acetic anhydride. Zinc chloride formed a stable, nonreactive complex with the β-aminocrotonic ester. We eliminated water from the reaction mixture by azeotropic distillation of water with dichloroethane during the reaction. The procedure proposed in the present work made it possible to raise the yields of 5-hydroxyindole derivatives noticeably. We obtained 2-methyl-3-carbethoxy-5-hydroxyindole (I), 1,2-dimethyl-3-carbethyoxy-5-hydroxindole (II), 1-phenyl-2-methyl-3-carbethoxy-5-hydroxyindole (III), 1-(o-tolyl)-2-methyl-3-carbethoxy-5-hydroxyindole (IV), 1-benzyl-2-methyl-3-carbethoxy-5-hydroxyindole (V), 1-(β'-hydroxyethyl)-2-methyl-3-carbethoxy-5-hydroxyindole (VI) and 1-phenyl-2-methyl-3-carbethoxy-5-hydroxybenzindole (VII).





(VII)



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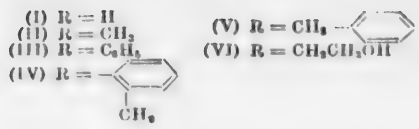
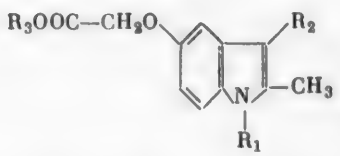


Methylation of (VI) with dimethyl sulfate gave 1-(β'-hydroxyethyl)-2-methyl-3-carbethoxy-5-methoxyindole (VIII).

In order to synthesize new plant growth stimulants, we studied the reaction of 5-hydroxyindoles with chloroacetic acid and bromoacetic ester. Treatment of (II) with monochloroacetic acid in the presence of 40% sodium hydroxide gave 1,2-dimethyl-3-carbethoxyindolyl-5-oxyacetic acid (IX) in good yield. Other 5-hydroxyindole derivatives could not be condensed with chloroacetic acid. The reaction solutions yielded the starting indoles and a substance whose properties were reminiscent of those of polyglycol resins. Apparently, even a slight decrease in the reactivity of 5-hydroxyindoles resulted only in hydrolysis of the chloroacetic acid to glycolic acid and the latter formed a polycondensation product under the reaction conditions. The phenolates of 5-hydroxyindole derivatives reacted with ethyl bromoacetate without complications. High yields of the substituted esters of indolyl-5-oxyacetic acids (X) and (XI) were obtained and hydrolysis of the esters gave the indolyl-5-oxyacetic acids (XII), (XIII) and (XIV).



(IX) $R_1 = CH_3$; $R_2 = COOC_2H_5$; $R_3 = H$
(X) $R_1 = H$; $R_2 = COOC_2H_5$; $R_3 = C_2H_5$
(XI) $R_1 = C_2H_5$; $R_2 = COOC_2H_5$; $R_3 = C_2H_5$
(XII) $R_1 = H$; $R_2 = COOC_2H_5$; $R_3 = H$
(XIII) $R_1 = C_2H_5$; $R_2 = COOH$; $R_3 = H$
(XIV) $R_1 = CH_2CH_2OH$; $R_2 = COOC_2H_5$; $R_3 = H$
(XV) $R_1 = CH_3$; $R_2 = H$; $R_3 = H$

Treatment of (IX) with sulfuric acid in an acetic acid solution by the method developed previously [9] gave 1,2-dimethylindolyl-5-oxyacetic acid (XV).

EXPERIMENTAL

2-Methyl-3-carbethoxy-5-hydroxyindole (I). 52.4 g (0.5 mole) of p-benzoquinone was dissolved in 500 ml of dichloroethane and 90.3 g (0.7 mole) of the ethyl β-aminocrotonate added to the solution obtained. The reaction solution was heated to boiling in a Wurtz flask and 350 ml of solvent distilled from it over 30-35 minutes (the solvent was distilled together with water liberated during the reaction). The residue was cooled and the crystals collected on a glass filter and sucked off. The mother solution, which was left to evaporate at room temperature for 2-3 days, deposited a precipitate and this was also collected. The crystals obtained were washed with ether on the filter and dried. The yield of (I) with m.p. 193-196° was 55 g (50.2%). After recrystallization from acetone, the product had m.p. 203-204°; according to literature data the m.p. is 205° [10].

Other 5-hydroxyindole derivatives were synthesized analogously (see table).

1-(β'-Hydroxyethyl)-2-methyl-3-carbethoxy-5-methoxyindole (VIII). 10.5 g of (VI) was dissolved in 20 ml of dioxane. To the solution obtained was added 40 ml of 2 N sodium hydroxide and 10.1 g of dimethyl sulfate. The reaction mixture was shaken at room temperature for 30 minutes and diluted with water. The crystals which separated on cooling were collected, washed with water and dried. The yield of (VIII) with m.p. 103-104° was 10 g (90%). After recrystallization from aqueous alcohol, the product had m.p. 106°.

Found %: C 65.18, 65.26; H 7.00, 6.96. $C_{15}H_{19}O_4N$. Calculated %: C 64.97; H 6.90.

1,2-Dimethyl-3-carbethoxyindolyl-5-oxyacetic acid (IX). 4.6 g of (II) was dissolved in 30 ml of dioxane. To the solution obtained was added 5.6 g of chloroacetic acid in the form of a 50% solution in water and 12 g of a 40% solution of sodium hydroxide. The reaction mixture was boiled for 40 minutes, cooled and diluted with a small amount of water. The crystals of the sodium salt precipitated were collected, washed with cold water and dried. The yield of the sodium salt was 6.3 g (85%). The salt was dissolved with heating in distilled water and acidified with 2 N hydrochloric acid to give (IX) with m.p. 196-197° (from acetone).

Found %: C 61.96, 61.85; H 5.86, 5.96. M 289. $C_{15}H_{17}O_5N$. Calculated %: C 61.84; H 5.88. M 291.3.

5-Hydroxyindole Derivatives

Starting materials	Indole obtained	Melting point		Yield (in %)		Found (%)		Calculated (%)	
		found	literature data	obtained	literature data	C	H	C	H
p-Benzoquinone and ethyl β-aminocrotonate	(I)	203—204°	205° [10]	50.2	28 [10]	—	—	—	—
p-Benzoquinone and ethyl N-methyl-β-aminocrotonate	(II)	208.5—209	207—208 [1]	60	48 [1]	—	—	—	—
p-Benzoquinone and ethyl N-phenyl-β-aminocrotonate	(III)	203—204	205—206 [10]	53.2	low [10]	—	—	—	—
p-Benzoquinone and ethyl N-o-tolyl-β-aminocrotonate	(IV)	208—209	208—209 [5]	54	24 [5]	—	—	—	—
p-Benzoquinone and ethyl N-benzyl-β-aminocrotonate	(V)	195	—	44		73.58, 73.66	6.28, 6.31	73.76	6.19
p-Benzoquinone and ethyl N-(β'-hydroxyethyl)-β-aminocrotonate	(VI)	174—175	—	46		63.79, 63.58	6.65, 6.58	63.86	6.51
α-Naphthoquinone and ethyl N-phenyl-β-aminocrotonate	(VII)	227—228	227 [5]	51.1	23.4 [5]				

Ethyl ester of 2-methyl-3-carbethoxyindolyl-5-oxyacetic acid (X). To an alcohol solution of sodium ethylate, prepared from 0.23 g of sodium and 20 ml of anhydrous alcohol, were added 2.2 g of (I) and 1.7 g of ethyl bromoacetate. The reaction mixture was boiled for 30 minutes, cooled and diluted with water. The precipitate was collected, washed with water and dried. The yield of material with m.p. 133-135° was 28 g (95%). After recrystallization from aqueous alcohol, (X) had m.p. 147-148°. The isomeric ethyl ester of 2-methyl-3-carbethoxy-5-hydroxyindole-1-acetic acid melted at 148° [10]. A mixture of the isomers melted over the range 121-129°.

Found %: C 62.72, 62.70; H 6.58, 6.47. $C_{16}H_{19}O_5N$. Calculated %: C 63.93; H 6.27.

Ethyl ester of 1-phenyl-2-methyl-3-carbethoxyindolyl-5-oxyacetic acid (XI). For the experiment we used a solution of sodium alcoholate, prepared from 14 ml of anhydrous alcohol and 0.23 g of sodium, 3 g of (III) and 1.7 g of ethyl bromoacetate. The reaction mixture was boiled for 1 hour. The processing and isolation of the substance was the same as in the previous experiment. The yield of (XI) with m.p. 142-145° was 3.6 g (94.4%). After recrystallization from alcohol, the product had m.p. 144.5-145.5°.

Found %:C 68.89, 69.09; H 6.35, 6.31. $C_{22}H_{23}O_5N$. Calculated %: C 69.27; H 6.08.

2-Methyl-3-carbethoxyindolyl-5-oxyacetic acid (XII). 1.52 g of (X) was dissolved in 20 ml of dioxane. To the solution obtained were added 1.4 g of potassium hydroxide and 2 ml of water. The reaction solution was boiled for 1 hour, diluted with water and acidified with 2 N hydrochloric acid. The precipitated crystals were collected and dried. The yield of (XII) was 1.2 g (85.7%). After recrystallization from water (with activated charcoal), the product had m.p. 207.5-208.5° (with decomp.).

Found %: C 60.88, 60.70; H 5.65, 5.76. M 276.4. $C_{14}H_{15}O_5N$. Calculated %: C 60.64; H 5.45. M 277.3.

1-Phenyl-2-methyl-3-carboxyindolyl-5-oxyacetic acid (XIII). The acid (XIII) was obtained by hydrolyzing ester (XI) under the conditions of the previous experiment. From 1.9 g of (XI) we obtained 1.4 g (87.5%) of the acid (XIII) with m.p. 176-176.5° (from alcohol).

Found %: C 66.23, 66.27; H 4.85, 4.73. M 328. $C_{18}H_{15}O_5N$. Calculated %: C 66.45; H 4.65. M 325.3.

1-(β '-Hydroxyethyl)-2-methyl-3-carbethoxyindolyl-5-oxyacetic acid (XIV). For the reaction we used a solution of sodium alcoholate prepared from 0.46 g of sodium and 25 ml of anhydrous alcohol, 6.3 g of (VI) and 3.34 g of ethyl bromoacetate. The reaction mixture was boiled for 30 minutes, diluted with water and the alcohol evaporated. The precipitated crystals (about 1 g) were collected together with the tar. Purification of them by recrystallization from methanol yielded the starting compound (VI) with m.p. 173-174.5°. Acidification of the mother solution with hydrochloric acid yielded 1 g of acid (XIV) with m.p. 189° (from methanol).

Found %: C 59.63, 59.78; H 6.08, 6.05. M 322. $C_{16}H_{19}O_6N$. Calculated %: C 59.80; H 5.96. M 321.3.

1,2-Dimethylindolyl-5-oxyacetic acid (XV). 1.5 g of (IX) was dissolved in acetic acid with heating. To the solution obtained was added 0.5 g of concentrated sulfuric acid as a 50% solution in acetic acid. The reaction mixture was boiled for 30 minutes and diluted with an equal volume of water. The precipitated crystals were collected washed with water and dried. The yield of (XV) was 0.8 g (72.7%) and the m.p. 198-199° (from aqueous acetone, 5:7). A mixture with the starting material melted at about 177°.

Found %: C 65.58, 65.64; H 6.03, 6.08. M 220. $C_{12}H_{13}O_2N$. Calculated %: C 65.74; H 5.98. M 219.2.

SUMMARY

1. It was shown that azeotropic distillation of water from the reaction mixture during the reaction of p-quinones with β-aminocrotonic ester and its analogs made it possible to increase the yield of 5-hydroxyindole derivatives considerably.

2. In order to synthesize plant growth stimulants, we studied the reaction of 5-hydroxyindoles with chloroacetic acid and bromoacetic ester.

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INVESTIGATION OF ACONITE ALKALOIDS

XV.* STRUCTURE OF ELATINE, METHYLLYCACONITINE, AJACINE, DELSEMINE, AVADHARIDINE, LYCACONITINE AND ELDELINE

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S. Ordzhonikidze All-Union Chemico-Pharmaceutical Scientific Research Institute

The study of polyhydroxylated alkaloids of Aconitum and Delphinium plants has advanced far in recent years and has led to the determination of the structures of many of them due to a large number of fine chemical investigations, among which, the work of Edwards et al. [1] and Cookson et al. [2] are outstanding. Very valuable data on the structure of the carbon skeleton of these substances were obtained by Przybylska [3] as a result of x-ray structural analysis.

The formula of lycoctonine (I) was put forward as early as 1956 [1]. However, the structure of such alkaloids as methyllycaconitine, ajacine, delsemine, avadharidine and lycaconitine, which are esters of lycoctonine, have remained undetermined until the present time since it was not established which of the three hydroxyl groups of the amino alcohol underwent esterification during formation of the ester. This problem may be solved by considering previously obtained data and a little experimental material of ours.

The alkaloid elatine [4] is an ester of the acid (II), whose structure we established [5, 6], and the amino alcohol, elatidine. By cleavage of the methylenedioxy group in elatine, this amino alcohol is converted into lycoctonine. Thus, elatidine differs from lycoctonine in the presence of a methylenedioxy group in place of the glycol group and consequently has the structure (III). Only one possible formula remains for elatine, namely (IV).

By heating elatine with dilute hydrochloric acid and phloroglucinol, we obtained the anthranilic ester of lycoctonine. The constants of this substance agreed with the constants of anthranoyllycoctonine obtained by cleavage of methyllycaconitine [7], delsemine [8], ajacine [9] and lycaconitine [10]. A direct comparison with the products of analogous cleavage of methyllycaconitine, which we made, showed the identity of the two bases.

Thus, for all the alkaloids listed above the primary hydroxyl group of lycoctonine was esterified with anthranilic acid. These alkaloids differ in the nature of the radical acylating the amino group of the anthranilic acid.

As is known, the alkaloid ajacine is N-acetylanthranoyllycoctonine (VI). The structure of the esterifying acid of methyllycaconitine was elucidated by R. Cookson et al. [11] simultaneously with our investigations of the structure of the esterifying acid of elatine. It was found that the two acids had the same structure (II). Hence, Formula (VII) may be proposed for methyllycaconitine.

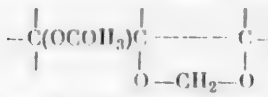
The alkaloid delsemine is formed from methyllycaconitine by the action of ammonia as a result of cleavage of the methylsuccinimido group and its conversion into a methylsuccinamido group [12]. The structure of the esterifying acid of delsemine (VIII) was established by S. Yu. Yunusov and N. K. Abubakirov [8]. The structure of delsemine may be represented by Formula (IX).

The alkaloid avadharidine [13] differs from delsemine only in that the former is a derivative of succinic and the latter a derivative of methylsuccinic acid. By acid cleavage of avadharidine, we obtained anthranoyllycoctonine. Consequently, avadharidine has structure (X). It might be thought that avadharidine is formed from

*For communication XIV see A. D. Kuzovkov, J. Gen. Chem. 29, 1728 (1959). See C. B. Translation.

lycaconitine by interaction with ammonia during the extraction of the alkaloids from the plant in the same way that delsemine is formed from methyllycaconitine. Apparently the esterifying acid of lycaconitine, like the esterifying acid of methyllycaconitine, contains a substituted succinimide grouping. Therefore, the structure of the former must be expressed by Formula (XI) and the structure of lycaconitine, by Formula (XII).

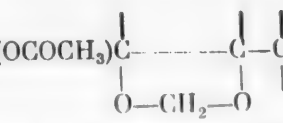
The alkaloid eldeline [14] is the acetyl ester of the amino alcohol eldelidine. By the action of hydrochloric acid on the latter, we obtained demethyleneeldelidine as a result of conversion of the methylenedioxy group into a glycol group [15]. A study of the periodic acid oxidation of eldeline, eldelidine and demethyleneeldelidine throws light on the relative positions of the acetoxy, methylenedioxy and hydroxyl groups on the alkaloid. While eldeline and eldelidine do not undergo oxidation, demethyleneeldelidine is cleaved by periodic acid at three carbon–carbon bonds. Hence, it follows that eldeline has the grouping



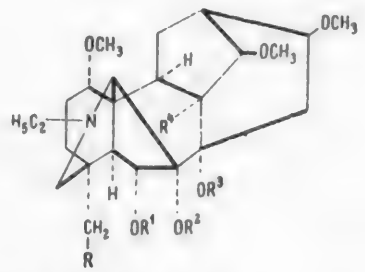
. The free hydroxyl group is extremely difficult to acetylate with acetyl chloride: after 4 hours' boiling the bulk of the eldeline remains unchanged. Treatment with chromium trioxide in acetic acid (6 days at 20°) also leads to recovery of part of the alkaloid unchanged. This hydroxyl group is apparently tertiary. The stability of eldelidine to reduction by $LiAlH_4$ and to catalytic hydrogenation with Pt (or PtO_2) shows that the tertiary hydroxyl is apparently not adjacent to the carbon atom with the nitrogen, as in hydroxylycoctonine [1].

Carmack et al. [16] recently isolated from Delphinium occidentale an alkaloid $C_{27}H_{41}O_8N$ with m.p. 193.5-194° and $[\alpha]_D$ −28.5°, which they called deltaline. Under the action of $SOCl_2$, the hydroxyl group in deltaline was replaced by chlorine. The chloro derivative obtained (m.p. 173-175°) was reduced with $LiAlH_4$ to desacetyldesoxydeltaline, which was found to be identical to the alkaloid delpheline. The following constants are given in the literature for this alkaloid and its salts and derivatives [2, 7]: base, m.p. 216-219°, $[\alpha]_D$ −25.8° ($CHCl_3$); $[\alpha]_D$ −42.8°; hydrochloride, m.p. 191-193°, $[\alpha]_D$ −41.2°; nitrate, m.p. 70-78°, $[\alpha]_D$ + 24° ($CHCl_3$); demethylenedelpheline, nitrate, m.p. 191-193°; perchlorate, m.p. 200°.

A comparison of the constants given above with the corresponding constants of eldeline and its derivatives shows that eldeline and deltaline are the same substances. Eldeline has the composition $C_{27}H_{41}O_8N$ and is characterized by m.p. 182-184° or (in vacuum at 0.1 mm) 192-193°; chloro derivative, m.p. 188-190° (from alcohol); desacetyldesoxyeldeline, m.p. 216.5-218°, $[\alpha]_D$ −22.9° ($CHCl_3$); hydrochloride, m.p. 218°, $[\alpha]_D$ −40.3°; nitrate, m.p. 177°, $[\alpha]_D$ −41.3°; demethylenedesacetyldesoxyeldeline, m.p. 69-75°; $[\alpha]_D$ + 30.0° ($CHCl_3$); perchlorate, m.p. 194°; nitrate, m.p. 191.5-192.5°.

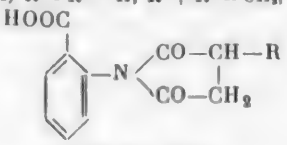
The structure of delpheline (XIII) was established by Cookson [2] In addition, Carmack et al. [16] converted delpheline through O-methyldelpheline into O-methyldemethylenedelpheline, which was found to be identical to desoxylycoctonine (XIV). The conversion of eldeline (deltaline) into delpheline consists of substituting hydrogen for the free hydroxyl in the grouping  , and hydrolyzing the acetoxy group.

The formula of delpheline (XIII) leads to the possible formula (XV) for eldeline and (XVI) for eldelidine.

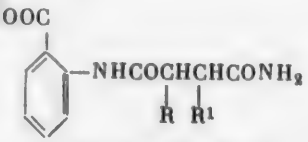


(I) R = OH, $R^1 = CH_3$, $R^2 = R^3 = R^4 = H$;
(III) R = OH, $R^1 = CH_3$, $R^2 + R^3 = CH_2$, $R^4 = H$;
(IV) R = $OCOC_6H_4NCOCH(CH_3)CH_2CO$, $R^1 = CH_3$, $R^2 + R^3 = CH_2$, $R^4 = H$;
(V) R = $OCOC_6H_4NH_2$, $R^1 = CH_3$, $R^2 = R^3 = R^4 = H$;
(VI) R = $OCOC_6H_4NHCOCH_3$, $R^1 = CH_3$, $R^2 = R^3 = R^4 = H$;
(VII) R = $OCOC_6H_4NCOCH(CH_3)CH_2CO$, $R^1 = CH_3$, $R^2 = R^3 = R^4 = H$;

(IX) R = $OCOC_6H_4NHCOCH(CH_3)CH_2CONH_2$ or $OCOC_6H_4NHCOCH_2CH(CH_3)CONH_2$, $R^1 = CH_3$, $R^2 = R^3 = R^4 = H$;
(X) R = $OCOC_6H_4NHCOCH_2CH_2CONH_2$, $R^1 = CH_3$, $R^2 = R^3 = R^4 = H$;
(XII) R = $OCOC_6H_4NCOCH_2CH_2CO$, $R^1 = CH_3$, $R^2 = R^3 = R^4 = H$;
(XIII) $R = R^1 = R^4 = H$, $R^2 + R^3 = CH_2$;
(XIV) $R = R^3 = R^2 = R^4 = H$, $R^1 = CH_3$;
(XV) R = H, $R^1 = OCOCH_3$, $R^2 + R^3 = CH_2$, $R^4 = OH$;
(XVI) $R = R^1 = H$, $R^2 + R^3 = CH_2$, $R^4 = OH$.



(II) R = CH_3;
(XI) R = H.



(VIII) R = CH_3, R^1 = H
or R = H, $R^1 = CH_3$.

EXPERIMENTAL

Anthranoyllycoctonine from elatine. 1 g of elatine, 0.5 g of phloroglucinol and 50 ml of hydrochloric acid (1 : 1) were heated for 1 hour at 90-92°, the red precipitate removed by filtration and the filtrate poured onto ice and carefully made alkaline with ammonia in the presence of ether. The layer of solvent was separated, rapidly dried and evaporated to small volume. We obtained 0.5 g of anthranoyllycoctonine with m.p. 159-161°. Mixed melting points with substances obtained from methyllycaconitine and avadharidine by the same method (but without phloroglucinol) were not depressed.

Action of thionyl chloride on eldeline. 90 ml of thionyl chloride was gradually added to 15 g of eldeline with cooling in ice water. When it had stood at 20° for 15 hours, the solution was boiled for 10 minutes and evaporated to dryness in vacuum and the residue dissolved in 50 ml of water. The solution was made alkaline with 40% sodium hydroxide solution and the base extracted with ether. A crystalline mass was obtained. Recrystallization from alcohol yielded 6 g of a substance with m.p. 188-190°.

Found %: C 60.66; H 7.65; N 2.66; Cl 6.91. $C_{27}H_{40}O_7NCl$. Calculated %: C 61.64; H 7.66; N 2.66; Cl 6.74.

Desacetyldesoxyeldeline (delpheline). A suspension of 2.8 g of the chloro derivative in 250 ml of dry ether and 1 g of lithium aluminum hydride was boiled for 18 hours with vigorous stirring. Recrystallization of the reaction product from acetone yielded 0.85 g of a substance with m.p. 216.5-218°; $[\alpha]_D$ −22.9° (c 2.8, $CHCl_3$).

Found C 67.11; H 8.82; N 3.06. $C_{25}H_{39}O_6N$. Calculated %: C 66.80; H 8.75; N 3.12.

The hydrochloride had m.p. 218° (from alcohol with ether), $[\alpha]_D$ −40.3° (c 2.1, water). The nitrate had m.p. 177° (from acetone), $[\alpha]_D$ −41.3° (c 4.5, water).

Demethylenedesacetyleldeline (demethylenedelpheline). The substance was obtained according to the description by Cookson [2]; it had m.p. 69-75° (from 50% methanol), $[\alpha]_D$ +30.0° (c 1.7, $CHCl_3$). The perchlorate had m.p. 194° (with decomp., from ethyl acetate); the nitrate had m.p. 191.5-192.5° (with decomp., from a mixture of acetone and ether).

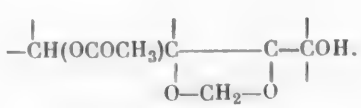
SUMMARY

1. A formula is proposed for the alkaloid elatine.

2. By conversion of elatine into anthranoyllycoctonine, we determined the position of the esterified hydroxyl in anthranoyllycoctonine and also in the alkaloids methyllycaconitine, delsemine, ajacine, avadharidine and lycaconitine, which are derivatives of anthranoyllycoctonine.

3. It was established that eldeline and deltaline are identical.

4. The presence of the grouping



in eldeline was demonstrated. A formula was proposed for eldeline.

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SOME PROPERTIES OF ENOL ACETATES

IV. NEW METHODS OF ALKYLATING CARBONYL COMPOUNDS

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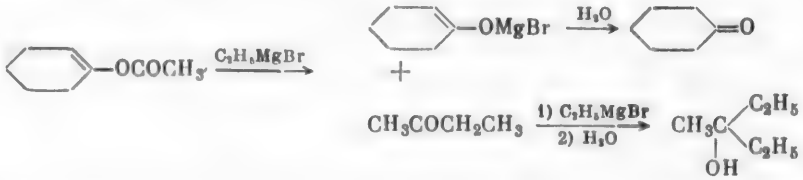
We recently showed that bromo-substituted enol acetates of aldehydes and ketones, which are readily prepared by the bromination of enol acetates with N-bromosuccinimide, may serve as starting materials for the synthesis of some furan and pyran derivatives [1-3]. In this work we developed a method of converting bromo-substituted enol acetates into monoalkyl derivatives of the corresponding carbonyl compounds by reacting bromo-substituted enol acetates with alkyl magnesium halides.

There were no data in the literature on the reaction of organomagnesium compounds with bromo-substituted enol acetates. A paper was recently published by Zwahlen et al. [4] on the reaction of unsubstituted enol acetates with alkyl magnesium halides and in it they showed that in the reactions of vinyl acetate, isopropenyl acetate and enol lactones with organomagnesium compounds, migration of the acyl group from the oxygen to the carbon occurred, followed by the formation of ditertiary glycols.

However, in our experiments on the reaction of cyclohexanone enol acetate with ethylmagnesium bromide we did not observe such a rearrangement and this enol acetate reacted with the organomagnesium compound like a normal ester. At a 2:1 molar ratio of ethylmagnesium bromide to cyclohexanone enol acetate, the reaction mixture yielded cyclohexanone (23% yield), methyldiethylcarbinol (35% yield) and an unsaturated ketone with the composition $C_{10}H_{16}O$ (25% yield). The ketone was apparently the product of crotonic condensation, formed during the reaction of methyl ethyl ketone with cyclohexanone (see Experimental for further details). When the reaction was carried out with equimolecular amounts of ethylmagnesium bromide and enol acetate, a 49% yield of cyclohexanone was obtained.

We thus established that in the case of cyclohexanone enol acetate, the latter reacted with ethylmagnesium bromide without the rearrangement, which would have been undesirable for our purposes, and with elimination of the enol acetate group and regeneration of the carbonyl group by the scheme

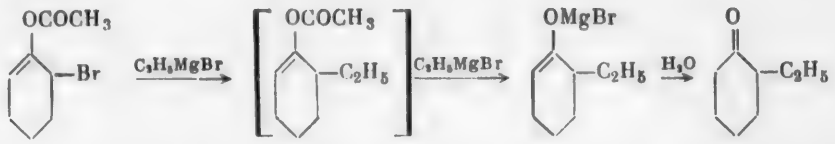


We studied the reaction of bromo-substituted enol acetates with organomagnesium compounds on the example of the reaction of ethylmagnesium bromide with bromo-substituted enol acetates of cyclohexanone, methyl propyl ketone, benzylacetone and butyraldehyde. The first of these bromo enol acetates contained the bromine atom in a position α and the rest in a position β to the carbonyl group of the original carbonyl compound.

At a 2:1 molar ratio of ethylmagnesium bromide and bromo-substituted enol acetate of cyclohexanone, the reaction gave a 60% yield of α-ethylcyclohexanone as the main product. A 3:1 molar ratio of these substances gave 1,2-diethylcyclohexanol-1 (40% yield).

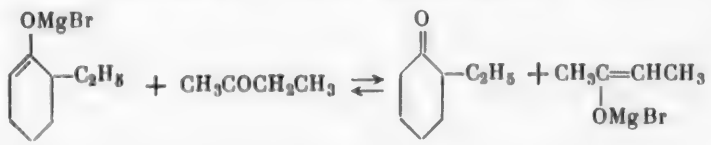
Ethylmagnesium bromide reacted similarly with the bromo-substituted enol acetates of methyl propyl ketone, butyraldehyde and benzylacetone. A 2:1 ratio of the starting reagents gave the corresponding β-ethyl carbonyl compounds, namely: 3-methylhexanone-5 (52% yield), 3-methylpentanal (41% yield) and 3-phenylhexanone-5 (44.9% yield); when the bromo-substituted enol acetates of methyl propyl ketone and butyraldehyde were reacted with a 3-fold amount of ethylmagnesium bromide, the corresponding alcohols were obtained: 3,5-dimethylheptanol-3 (60% yield) and 3-methylheptanol-5 (74.5% yield).

The formation of an alkylated carbonyl compound from a bromo enol acetate by treating it with an organomagnesium compound (for example 3-bromocyclohexenyl acetate) may be represented by the following scheme:



The great lability of the bromine atom in a bromo-substituted enol acetate * should be noted as it is precisely the halogen atom in the latter that first exchanges for the radical of the organomagnesium compound in contrast to halocarboxylic esters where the ester group is cleaved first and only then does the halogen atom react (usually under different conditions).

The formation of a tertiary alcohol (at a molar ratio of Grignard reagent to bromo enol acetate of 3:1) may be understood readily if one assumes that the magnesium enolate bromide of α-ethylcyclohexanone and methyl ethyl ketone first formed react with each other by a type of "transenolization"



and then the cyclic ketone reacts with the organomagnesium compound in the usual way.

The method we developed makes it possible to α-alkylate ketones under mild conditions to give bromo-substituted enol acetates of the type $RCH=C(OCOCH_3)-CHBr-R^1$ and to β-alkylate carbonyl compounds to give bromo enol acetates of the type $R-CHBr-CH=C(OCOCH_3)-R^1$ (for aldehydes $R^1=H$ and for methyl ketones $R^1=CH_3$). The advantage of this method is the formation of monoalkylation products of the starting carbonyl compounds with the alkyl group in a strictly determined position and without traces of polyalkyl derivatives. This method may be used in fine organic synthesis.

EXPERIMENTAL

1. Interaction of enol acetate of cyclohexanone with ethylmagnesium bromide. The reaction was carried out in a three-necked flask with a stirrer, a dropping funnel and a reflux condenser, fitted with a tube filled with a mixture of soda lime and calcium chloride. The Grignard reagent was prepared from 14.6 g of Mg (0.6 g-atom), 68.6 g of C_2H_5Br (0.63 mole) and 100 ml of absolute ether. At the end of the reaction, the mixture was heated with the ether boiling for 30 minutes. The cooled ether solution of the Grignard reagent was slowly added with vigorous stirring to a solution of 42.1 g (0.3 mole) of the enol acetate of cyclohexanone (b.p. 52-53° at 5 mm) in 100 ml of ether. When the Grignard reagent had been added, the flask was heated on a water bath with the ether boiling for 3 hours, then cooled with cold water and a saturated aqueous solution of ammonium chloride added slowly with vigorous stirring until the initially precipitated magnesium salts dissolved completely. After separation of the ether layer, the reaction product was extracted from the aqueous layer many times with ether; the combined ether extracts were dried with sodium sulfate and the solvent removed; distillation of the residue at atmospheric pressure yielded 10.7 g (35%) of a fraction of methyldiethylcarbinol.

* We had assumed this, considering the position of the bromine atom with respect to the double bond ("allyl").

B.p. 122-124°, $n^{20}D$ 1.4191, d^{20}_4 0.8193, MR_D 31.51; calc. 31.43. Literature data: b.p. 121-123°, $n^{21}D$ 1.4180, d^{20}_0 0.8237 [5].

Found %: C 70.21, 70.06; H 13.42, 13.46; OH (according to Tserevitinov's method) 16.25. $C_6H_{14}O$. Calculated %: C 70.53; H 13.81; OH 16.67.

After distillation of the methyldiethylcarbinol, the residue was vacuum distilled at 5 mm; this yielded the following substances.

a) Cyclohexanone (6.8 g, 23%).

B.p. 25-27° (5 mm), 155-156° (760 mm), $n^{20}D$ 1.4485, d^{20}_4 0.9518, MR_D 27.61; calc. 27.72. Ketone content (found by oximination) 98.2%. Literature data: $n^{20}D$ 1.4503, d^{20}_4 0.9473 [6].

Found %: C 73.42, 73.55; H 10.75, 10.67. $C_6H_{10}O$. Calculated %: C 73.43; H 10.27.

b) An unsaturated ketone (11.1 g).

B.p. 80-82° (3 mm), $n^{20}D$ 1.4913, d^{20}_4 0.9722, MR_D 45.41; calc. 45.72. Ketone content 97.5%.

Found %: C 78.56, 78.48; H 10.75, 10.67. M 148.3. Bromine number 98.2. $C_{10}H_{16}O$. Calculated %: C 78.89; H 10.59; M 152.23. Bromine number 104.9.

The semicarbazone had m.p. 246° (from alcohol).

Found %: N 20.32, 20.45. $C_{11}H_{19}ON_3$. Calculated %: N 20.08.

This unsaturated ketone was probably the product of crotonic condensation of methyl ethyl ketone and cyclohexanone. From literature data it is known that the condensation of these ketones in the presence of sodium ethylate forms two isomeric ketones, cyclohexenylmethyl ethyl ketone and cyclohexylidenemethyl ethyl ketone, whose constants differ considerably from the constants of the unsaturated ketone we isolated [7-9].

2. Preparation of α-ethylcyclohexanone. A Grignard reagent was prepared from 4.86 g of Mg (0.2 g-atom), 22.1 g of C_2H_5Br, (0.23 mole) and 100 ml of absolute ether; at the end of the reaction the mixture was heated for 30 minutes on a water bath with the ether boiling. The cooled solution of Grignard reagent was added dropwise with vigorous stirring to a solution of 21.9 g (0.1 mole) of 3-bromo-2-acetoxycyclohexene (b.p. 82-84° at 5 mm) in 50 ml of ether. A voluminous white precipitate formed immediately. The mixture was then heated and stirred for 5 hours on a water bath at the boiling point. The mixture was cooled and a saturated solution of NH_4Cl added dropwise until the initially precipitated magnesium salts dissolved. After many extractions with ether, the combined ether extracts were dried with sodium sulfate and the solvent removed in vacuum. Fractionation in vacuum yielded α-ethylcyclohexanone (7.6 g, 60%).

B.p. 52-54° (3 mm), $n^{20}D$ 1.4555, d^{20}_4 0.939, MR_D 36.85; calc. 36.96. Ketone content 95.5%. Literature data: b.p. 67° (12 mm) [10], $n^{20}D$ 1.4522 [11], $n^{20}D$ 1.4557 [12], d^{20}_4 0.919 [11].

Found %: C 75.85, 75.76; H 11.35, 11.51. $C_8H_{14}O$. Calculated %: C 76.14; H 11.18.

Semicarbazone: m.p. 158° (from benzene); literature data: m.p. 161° [13].

Found %: N 23.25, 23.14. $C_9H_{17}ON_3$. Calculated %: N 22.93.

2,4-Dinitrophenylhydrazone: m.p. 136° (from a mixture of alcohol and ethyl acetate). Literature data: m.p. 133-134° [12], 164-166° [14].

Found %: N 18.06, 17.99. $C_{14}H_{18}O_4N_4$. Calculated %: N 18.29.

3. Preparation of 1,2-diethylcyclohexanol-1. A Grignard reagent was prepared from 7.29 g of Mg (0.3 g-atom), 36.0 g of C_2H_5Br (0.33 mole) and 125 ml of absolute ether and added to a solution of 21.9 g (0.1 mole) of 3-bromo-2-acetoxycyclohexene-1 in 50 ml of ether. The reaction and processing were as in the previous experiment. Fractionation in vacuum yielded 1,2-diethylcyclohexanol-1 (6.3 g, 40% yield).

B.p. 73.5-74.5° (3 mm), $n^{20}D$ 1.4625, d^{20}_4 0.911, MR_D 47.15; calc. 47.71. Literature data: b.p. 72-73° (3 mm) [15], $n^{20}D$ 1.4665, d^{20}_4 0.918 [12].

Found %: C 76.52, 76.69; H 13.12, 13.05; OH 11.05, 11.10. M 154.2. $C_{10}H_{20}O$. Calculated %: C 76.86; H 12.90; OH 10.9. M 156.26.

α-Ethylcyclohexanone was not detected among the reaction products.

4. Preparation of 3-methylhexanone-5. The Grignard reagent was prepared as usual from 4.86 g of Mg (0.2 g-atom), 22.1 g of C_2H_5Br (0.23 mole) and 100 ml of absolute ether and added to a solution of 20.7 g (0.1 mole) of 4-bromo-2-acetoxypentene-2 (b.p. 46-48° at 4 mm) in 50 ml of ether. The synthesis and processing were as in the preparation of α-ethylcyclohexanone. Vacuum distillation yielded 3-methylhexanone-5 (5.9 g, 52%).

B.p. 36-38° (14 mm), $n^{20}D$ 1.4095, d^{20}_4 0.815, MR_D 34.64; calc. 34.54. Ketone content 98.4%. Literature data: b.p. 35-37° (11 mm) [16], $n^{25}D$ 1.4050, d^{20}_4 0.8085 [17].

Found %: C 73.41, 73.52; H 12.64, 12.58. $C_7H_{14}O$. Calculated %: C 73.63; H 12.36.

Semicarbazone: m.p. 123° (from aqueous alcohol). Literature data: m.p. 126-127° [18].

Found %: N 24.72, 24.65. $C_8H_{17}ON_3$. Calculated %: N 24.54.

5. Preparation of 3,5-dimethylheptanol-3. The Grignard reagent was prepared from 7.29 g of Mg (0.3 g-atom), 36.0 g of C_2H_5Br (0.33 mole) and 125 ml of absolute ether and added to a solution of 20.7 g (0.1 mole) of 4-bromo-2-acetoxypentene-2 in 50 ml of ether. The reaction mixture was boiled for 8 hours. Processing was as in previous experiments. Vacuum distillation yielded 3.5-dimethylheptanol-3 (8.65 g, 60%).

B.p. 49-51° (15 mm), $n^{20}D$ 1.4325, d^{20}_4 0.824, MR_D 45.42; calc. 45.28. Literature data: b.p. 88.4-88.6° (35 mm), $n^{24}D$ 1.4317, d^{24}_4 0.833 [19].

Found %: C 74.68, 74.75; H 14.08, 14.21; OH 11.92. M 141.3. $C_9H_{20}O$. Calculated %: C 74.93; H 13.98; OH 11.79. M 144.2.

6. Preparation of 3-phenylhexanone-5. The Grignard reagent was prepared from 4.86 g of Mg (0.2 g-atom), 22.1 g of C_2H_5Br (0.23 mole) and 100 ml of absolute ether and added to a solution of 26.9 g (0.1 mole) of 1-bromo-1-phenyl-3-acetoxybutene-2 in 50 ml of ether. After the addition of the Grignard reagent, the reaction mixture was heated for 1 hour. The usual processing yielded 3-phenylhexanone-5 (7.9 g, 44.9%).

B.p. 105-106° (1 mm), $n^{20}D$ 1.5202, d^{20}_4 0.9959, MR_D 54.02; calc. 53.85. Ketone content 98.2%. Literature data: b.p. 130° (18 mm) [20].

Found %: C 81.55, 81.49; H 9.34, 9.47. $C_{12}H_{16}O$. Calculated %: C 81.77; H 9.15.

Semicarbazone: m.p. 252° (from aqueous alcohol).

Found %: N 18.15. $C_{13}H_{19}ON_3$. Calculated %: N 18.01.

7. Preparation of 3-methylpentanal-1. a) Preparation of enol acetate of butyraldehyde. 72.1 g (1.0 mole) of butyraldehyde (b.p. 75-76°), 153.1 g (1.5 mole) of acetic anhydride and 12.3 g (0.125 mole) of fused potassium acetate were boiled on an oil bath for 4 hours in a flask with a reflux condenser. The reaction mixture was then cooled, the excess acetic anhydride decomposed by shaking with water, the oily layer separated and the aqueous layer neutralized with solid sodium carbonate and then extracted many times with ether. The ether extracts were added to the oil, washed with 15% Na_2CO_3 solution until weakly alkaline to litmus and then with water and dried over sodium sulfate and the ether removed. Distillation yielded the two following substances.

1) Enol acetate of butyraldehyde (51.9 g).

B.p. 128-130°, $n^{20}D$ 1.4170, d^{20}_4 0.9361, MR_D 30.71; calc. 31.10.

Found %: C 63.19, 63.05; H 8.76, 8.69. Saponification number 482; bromine number 133.1. $C_6H_{10}O_2$. Calculated %: C 63.30; H 8.79. Saponification number 489; bromine number 139.5.

The enol acetate of butyraldehyde has not been described in the literature.

2) Diacetate of butyraldehyde (58.3 g).

B.p. 185-190°. Saponification number 621; calc. 643.

The diacetate of hydrated butyraldehyde has not been described in the literature.

b) Bromination of enol acetate of butyraldehyde with N-bromosuccinimide. A mixture of 11.5 g (0.1 mole) of the enol acetate of butyraldehyde, 17.8 g (0.1 mole) of N-bromosuccinimide and 30 ml of CCl_4 were heated on a water bath under reflux. At a bath temperature of 76°, a vigorous reaction began in the flask and heating was stopped. The mixture was cooled, the precipitated succinimide removed, and the precipitate washed with CCl_4 and the filtrate washed many times with water and dried with sodium sulfate. The solvent was then removed with vacuum. Vacuum distillation yielded 2-bromo-4-acetoxybutene-3 (6.7 g, 34.6%).

Found%: Br 41.09, 39.95. $C_6H_9O_2Br$. Calculated %: Br 41.28.

c) Preparation of 3-methylpentanal-1. The Grignard reagent was prepared as usual from 4.86 g of Mg (0.2-g-atom), 22.1 g of C_2H_5Br (0.23 mole) and 100 ml of absolute ether and added to a solution of 19.3 g (0.1 mole) of 2-bromo-4-acetoxybutene-3 in 50 ml of ether. The mixture was boiled for 10 hours. The usual processing and vacuum distillation yielded 3-methylpentanal-1 (4.16 g, 41.0%).

B.p. 38-40° (32 mm), n_D^{20} 1.4070, d_4^{20} 0.8262, MR_D 29.86; calc. 29.92. Aldehyde content 97.8 %. Literature data: m.p. 35-36° (28 mm), n_D^{20} 1.4019 [21].

Found %: C 71.75, 71.67; H 12.12, 12.01. $C_6H_{12}O$. Calculated %: C 71.94; H 12.08.

Semicarbazone: m.p. 125° (from aqueous alcohol); literature data: m.p. 128-129° [22], 126-127° [21].

Found %: N 26.98. $C_7H_{15}ON_3$. Calculated %: N 26.73

8. Preparation of 3-methylheptanol-5. The Grignard reagent was prepared from 7.29 g of Mg (0.3 g-atom), 36.0 g of C_2H_5Br (0.33 mole) and 125 ml of absolute ether and added to a solution of 19.3 g (0.1 mole) of 2-bromo-4-acetoxybutene-3 in 50 ml of ether. The reaction mixture was boiled for 12 hours. Processing was as in the previous experiments. Vacuum distillation yielded 3-methylheptanol-5 (9.7 g, 74.5%).

B.p. 70-72° (28 mm), n_D^{20} 1.4233, d_4^{20} 0.8290, MR 39.98; Calc. 40.67. Literature data: b.p.: 167-168° (760 mm) [23].

Found %: C 73.56, 73.65; H 13.78, 13.62; OH 12.94, 13.02. $C_8H_{18}O$. Calculated %: C 73.78; H 13.93; OH 13.06.

SUMMARY

1. A method was developed for the monoalkylation of carbonyl compounds by reacting the bromo-substituted enol acetates, readily prepared from them, with organomagnesium compounds.

2. It was shown that on reacting bromo enol acetates with organomagnesium compounds in molar ratios of 1:2, in addition to replacement of the halogen atom by alkyl, decomposition of the enol acetate group occurred with the formation of a carbonyl group. At a 1:3 molar ratio of the reagents, the corresponding tertiary alcohols were formed as the main product.

3. The bromo enol acetate of cyclohexanone (the bromine was in a position α to the original carbonyl group) reacted with ethylmagnesium bromide to give α-ethylcyclohexanone (at a molar ratio of 1:2) and 1,2-diethylcyclohexanol-1 (at a molar ratio of 1:3). Bromo-substituted enol acetates of methyl propyl ketone, benzylacetone and butyraldehyde (the bromine atom in a position β to the original carbonyl group) reacted with ethylmagnesium bromide at a molar ratio of 1:2 to give products of β-ethylation of the starting carbonyl compounds: 3-methylhexanone-5, 3-phenylhexanone-5 and 3-methylheptanal-1. With a 1:3 ratio of the brominated enol acetates of methyl propyl ketone and butyraldehyde to the Grignard reagent, 3,5-dimethylheptanol-3 and 3-methylheptanol-5 were obtained.

4. It was shown that in contrast to vinyl acetate and isopropenyl acetate, which according to the data of Zwahlen et al. undergo rearrangement under the conditions of the Grignard reaction, the enol acetate of cyclohexanone reacted with ethylmagnesium bromide similarly to a normal ester.

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MONOMETHYNE DYES OF THE INDOLICINE SERIES

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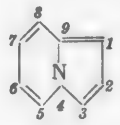
Despite the high reactivity of indolicine (I)* and the developed system of conjugated bonds in its molecule, very few dyestuffs based on it have been described. There have mainly been patent descriptions [1] containing insufficient basic data on the structure of the dyes. For example, dyes obtained from 2-substituted indolicines have been arbitrarily ascribed a structure according to which the external polymethyne chain occupies position 3. Meanwhile, it is known that position 1 of the indolicine molecule has a particularly high activity with respect to electrophilic reagents [2, 4, 5].

(I)

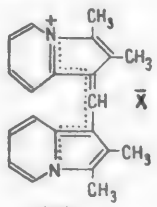


(II)

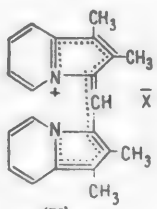
The aim of the present work was to demonstrate the possibility in principle of preparing two series of indolicine dyes with the external chain in positions 1 and 3 and to compare their spectra properties. So as to fix the external chain in a definite position, in the experiments described below we started from disubstituted indolicines with one free position in the five-membered ring.

The condensation of 1,2-dimethylindolicine with orthoformic ester in an acetic acid medium in the presence of potassium bromide led to the formation of the salt of a basic dye, to which the structure (IIIa) could be ascribed unequivocally. The less soluble and more readily crystallizable perchlorate of this dye (IIIb) was obtained by heating the perchlorate of 1,2-indolicine with orthoformic ester in pyridine.

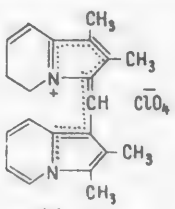
An analogous condensation of 2,3-dimethylindolicine in the presence of potassium iodide led to the formation of the dye (IVa).



(III)
a) X = Br⁻
b) X = ClO4⁻



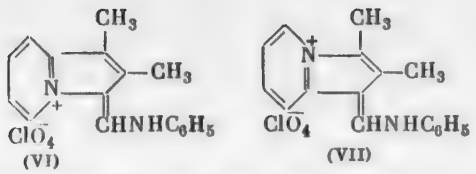
(IV)
a) X = I⁻
b) X = ClO4⁻



(V)

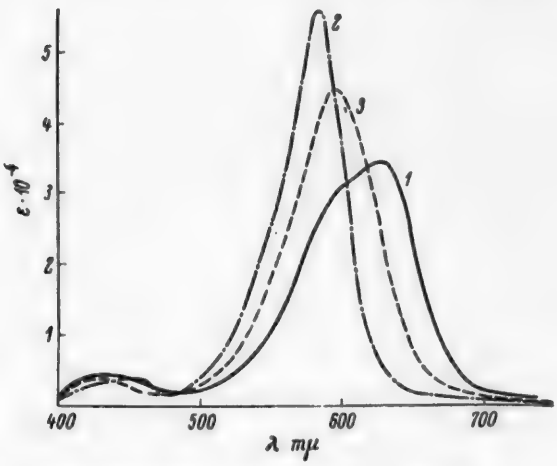
A possible synthesis of the unsymmetrical dye (V) is as follows. Condensation of 2,3-dimethylindolicine perchlorate with diphenylformamide in acetic anhydride led to the anilinomethylene derivative (VI). When this substance was heated with 1,2-dimethylindolicine in butanol, dye (V) was

*The name "indolicine" and the numbering shown were first used in the work of Soviet authors [2] and are based on the isomeric relation of the substance to indole and the degree of reactivity of the different positions in its molecule. The same nomenclature is accepted in German and Japanese literature. The name "pyrrocoline" and the numbering (II), which is accepted in U.S.A. and Britain, shows only the relation of this substance to picoline and the method by which it was first prepared [3].



formed. Condensation of 1,2-dimethylindolicine with diphenylformamide yielded the analogous anilinomethylene derivative (VII).

The absorption curves of the three dyes obtained are shown in the figure. Dye (III) has a maximum at the shortest wavelengths. This is in accord with the fact that it has the shortest conjugated chain between the nitrogen atoms, which includes 5 carbon atoms [shown by a dotted line in Formula (III)]. The position of the absorption maximum (587 mμ in alcohol solution) lies within the limits of this value for many polymethyne dyes with a conjugated chain of equal length (from 550 mμ for ethyl red to 604 mμ for pinacyanol). The extinction value of 56,000 is somewhat lower than that for dyes corresponding in length of conjugated chain with one external carbon atom (ethyl red ε 92,000). However, on going to dye (IV) a considerable derivation from known rules was observed. Dye (IV) has a conjugated chain of 9 carbon atoms and in analogy with known relations for quinoline dyes (change from pseudocyanines to cyanines), it should have an absorption maximum at 680-690 mμ. In actual fact it has an absorption maximum at 629 mμ. The asymmetric dye (V) absorbs in an intermediate region, but its absorption maximum is displaced from the arithmetic mean of the values for the two symmetrical dyes by 12 mμ toward shorter wavelengths. This is reminiscent of the relation for unsymmetrical dyes with hetero atoms, differing considerably in basicity. Such an analogy has certain structural foundations: dye (III) may be considered as a pyridine derivative and (IV) is undoubtedly a pyrrole derivative. It would have been interesting to compare the basicities of the two symmetrical dyes [6], but these dyes were not decolorized by acids. Some light might be shed by a study of indolicine dyes containing greater numbers of carbon atoms in the external chain; our next communication will be devoted to this problem.



Absorption spectra in alcohol. 1) Dye (IVa); 2) dye (IIIa); 3) dye (V).

EXPERIMENTAL

1-Anilinomethylene-2,3-dimethylindolicine perchlorate (VI). 0.49 g of 2,3-dimethylindolicine perchlorate, 0.38 g of diphenylformamide and 8 ml of acetic anhydride were mixed in the cold. After 2-3 minutes, the solution formed deposited a crystalline precipitate. The substance was recrystallized from alcohol. The golden yellow needles had m.p. 262-263° (decomp.). The yield was 0.43 g (61%).

Found %: N 8.01, 7.95. $C_{17}H_{17}O_4N_2Cl$. Calculated %: N 7.85.

3-Anilinomethylene-1,2-dimethylindolicine perchlorate (VII). The substance was obtained analogously to (VI). The yield was 56%. The yellow needles from alcohol had m.p. 265-270° (decomp.).

Found %: N 8.03, 7.76. $C_{17}H_{17}O_4N_2Cl$. Calculated %: N 7.85.

Bis-(2,3-dimethylindolicyl-1)-methene perchlorate (IVb). A mixture of 0.1 g of 2,3-dimethylindolicine and 0.28 g of (VI) was dissolved with heating in 4 ml of butanol and boiled for 2.5 hours. The dye which precipitated on cooling was washed successively with alcohol, water, alcohol and ether. The dark blue, crystalline powder had λ_{max} 629 mμ. The yield was 0.2 g (74%).

Found %: N 7.21, 7.14. $C_{21}H_{21}O_4N_2Cl$. Calculated %: N 6.99.

Iodide (IVa). A mixture of 1.1 g of 2,3-dimethylindolicine, 1.1 g of orthoformic ester, 1.5 g of potassium iodide and 4 ml of glacial acetic acid was boiled for 10 minutes. To the cooled mixture was added 5 ml of alcohol and the solution obtained was poured into 100 ml of ice-cooled ether. The precipitated dye was recrystallized several times from alcohol. The bronze-green needles had m.p. 293-294° (decomp.) and λ_{max} 629 mμ (in alcohol).

Found %: N 6.46, 6.53. $C_{21}H_{21}N_2I$. Calculated %: N 6.54.

Bis-(1,2-dimethylindolicyl-3-)methene bromide (IIIa). A mixture of 1.45 g of 1,2-dimethylindolicine, 1.48 g of orthoformic ester, 1.25 g of potassium bromide and 12 ml of acetic anhydride was boiled for 30 minutes. The precipitate formed on cooling to 0° (1.19 g) was recrystallized twice from alcohol. We obtained 0.83 g (44%) of a bronze, crystalline substance with m.p. 260-262° (decomp.) and λ_{max} 587 mμ (in alcohol).

Found %: N 7.69, 7.64. $C_{21}H_{21}N_2Br$. Calculated %: N 7.34.

Perchlorate (IIIb). A mixture of 0.46 g of 1,2-dimethylindolicine perchlorate, 0.56 g of orthoformic ester and 4 ml of pyridine was boiled for 2 hours. The cooled solution was diluted with an equal volume of water. The precipitated dye was recrystallized twice from alcohol. The dark blue, crystalline powder had m.p. 270-273° (decomp.) and λ_{max} 587 mμ (in alcohol). The yield was 0.2 g (53.2%).

Found %: N 7.12, 7.22. $C_{21}H_{21}O_4N_2Cl$. Calculated %: N 6.99.

(1,2-Dimethylindolicyl-3)-(2,3-dimethylindolicyl-1-)methene perchlorate (V). A mixture of 0.115 g of (VI), 0.06 g of 1,2-dimethylindolicine and 3 ml of butanol was boiled for 1.5 hours. On cooling, the reaction mixture deposited the dye (0.082 g). After two recrystallizations from alcohol, the substance weighed 0.041 g (35.6%) and had m.p. 289-291° (decomp.) and λ_{max} 596 mμ (in alcohol).

Found %: N 7.06, 7.07. $C_{21}H_{21}O_4N_2Cl$. Calculated %: N 6.99.

SUMMARY

1. Indolicine forms two series of methyne dyes with an external chain in two positions of the five-membered ring. Mixed dyes may also be obtained.

2. The spectral properties of the dyes obtained were investigated.

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* Institute of Organic Chemistry.

SYNTHESIS OF THIAZOLIDONE DERIVATIVES OF BIOLOGICAL INTEREST

XIII. CONVERSION OF RHODANINES INTO THIAZOLIDINEDIONES-2,4

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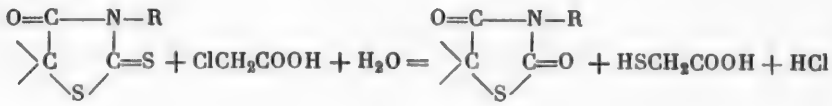
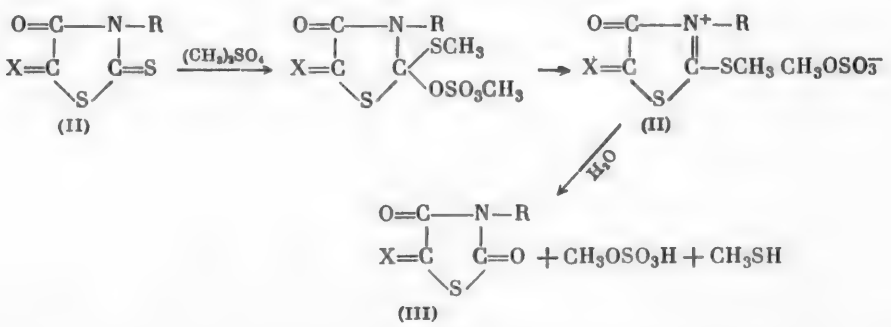
The conversion of rhodanines into thiazolidinediones-2,4 involves a series of difficulties. Klason [1] showed that when rhodanine was heated with hydrochloric acid in a sealed tube at 130°, hydrolysis occurred and in addition to thioglycolic acid, thiazolidinedione-2,4 was formed as a side product. Kitamura [2, 3] replaced the S atom in position 2 of the rhodanine molecule and its 5-arylidene derivatives with an O atom by oxidation with perhydrol in an alkaline medium. The oxidation reaction proceeded readily, but the thiazolidinediones formed very rapidly underwent further oxidation to form sulfacetamide, $H_2NCOCH_2SO_2H$. Oxidation of 5-benzylidenerhodanine yielded benzoic acid. The reactions of Klason and Kitamura cannot be used for the preparative conversion of rhodanines into thiazolidinediones. The indirect method proposed by N. M. Turkevich et al. [4-6] give reasonable results. Due to the thioketonic character of the sulfur atom in position 2, rhodanine reacts with hydrazine and its derivatives (semicarbazide, thiosemicarbazide, phenylhydrazine etc.) to form pseudothiohydantoin derivatives. The latter substances are readily converted into thiazolidinediones-2,4 by acid hydrolysis. However, the proposed method is very laborious.

We turned to a method which is frequently used for converting 2-thiohydantoins into hydantoins [7], and is based on prolonged boiling of preparations with monochloroacetic acid. This method was used by Croxall et al. [8] for converting rhodanine and its 5-isopropylidene, 5-sec -butylidene and 5-cyclohexylidene derivatives into the corresponding thiazolidinediones-2,4 in 38-77% yield. Our experiments showed that this method may only be applied to rhodanines which are more or less soluble in water (e.g., unsubstituted rhodanine and 3-phenylrhodanine). The method cannot be applied to 5-arylidenerhodanines since these substances are practically insoluble in aqueous solutions of monochloroacetic acid. The reaction of monochloroacetic acid with rhodanines may be represented by the scheme:



We obtained much better results by heating rhodanine derivatives with dimethyl sulfate without solvent. The mechanism of the reaction may be represented by the following scheme:



This reaction was carried out by Z. P. Sytnik et al. [9] for certain merocyanine dyes based on rhodanine, and the intermediate reaction products (II) were isolated.

We showed that the conversion of rhodanines into thiazolidinediones by means of dimethyl sulfate has a general character and may be used for rhodanines substituted in position 3 or 5. The substance investigated was heated with excess dimethyl sulfate at 120-140° and the reaction product (II) was hydrolyzed by boiling with dilute alcohol. The reaction proceeded in good yield (54-92%) and in most cases the uncrystallized final reaction product differed little in melting point from the chemically pure substance. In the reaction of dimethyl sulfate with rhodanines unsubstituted in position 3, methylation in this position occurred simultaneously.

Some of the thiazolidinediones-2,4 we synthesized, in particular the 3-p-ethoxyphenyl derivative, had a marked tuberculostatic action.

EXPERIMENTAL

3-Phenylthiazolidinedione-2,4 [(III), $R=C_6H_5$, $X=H_2$]. 4.0 g of 3-phenylrhodanine was boiled in 300 ml of a 27% solution of monochloroacetic acid in a flask with a reflux condenser for 20 hours. During the boiling, the starting material gradually dissolved. The boiling solution was filtered and the filtrate cooled. The precipitate which formed in the cold was collected, washed with water and dried. We obtained 2.4 g (65.0%) of an almost colorless, crystalline product with m.p. 137°; a mixed melting point with a preparation (m.p. 143°) obtained by acid hydrolysis of 3-phenylpseudothiohydantoin was not depressed.

3-Phenyl-5-benzylidenethiazolidinedione-2,4 [(III), $R=C_6H_5$, $X=C_6H_5CH$]. 3.0 g (10.1 mmole) of 3-phenyl-5-benzylidenerhodanine was mixed with 3.8 ml (40 mmole) of dimethyl sulfate and heated in a flask under reflux at 120-140° (inside reaction mixture). During the heating a solution was formed and gas was gradually evolved. The reaction mixture was left overnight at room temperature and then treated twice with ether (20 ml portions) to remove excess dimethyl sulfate. The residue, a thick, dark mass, was boiled with 50 ml of dilute alcohol (1:1) for 30 minutes. During the boiling a precipitate was formed. After cooling, the precipitate was collected, washed with water and dried. We obtained 2.6 g (91.8%) of an almost colorless substance with m.p. 208-209°. A mixed melting point with a preparation (m.p. 208°) obtained by heating 3-phenylthiazolidinedione-2,4 with benzaldehyde [10] was not depressed.

When 3-phenyl-5-benzylidenerhodanine was boiled with an aqueous solution of monochloroacetic acid and also when these substances were fused together (without solvent), 3-phenyl-5-benzylidenethiazolidinedione-2,4 was not isolated from the reaction products.

3-Methyl-5-benzylidenethiazolidinedione-2,4 [(III), $R=CH_3$, $X=C_6H_5CH$]. 3.0 g of 5-benzylidenerhodanine was reacted with dimethyl sulfate as described above. We obtained 1.8 g (60.6%) of a yellowish, crystalline substance with m.p. 130°, which did not depress the melting point of a preparation (m.p. 133°) obtained according to Dains et al. [11].

We obtained an identical product with m.p. 132-134° in 90% yield by heating 3-methyl-5-benzylidenerhodanine [(1), $R=CH_3$, $X=C_6H_5CH$] with dimethyl sulfate and subsequent hydrolysis of the intermediate reaction product.

3-p-Ethoxyphenylthiazolidinedione-2,4 [(III), $R=C_2H_5OC_6H_4$, $X=H_2$] was obtained analogously from 3-p-ethoxyphenylrhodanine and dimethyl sulfate in 54.1% yield (after recrystallization from alcohol, the product had m.p. 152°). The 5-benzylidene derivative was obtained from 3-p-ethoxyphenyl-5-benzylidenerhodanine in 63.8% yield after recrystallization from glacial acetic acid, the produce had m.p. 192°). Mixed melting points of the substances obtained with preparations obtained by acid hydrolysis of appropriate pseudothiohydantoin derivatives were not depressed.

SUMMARY

1. Rhodanines may be converted into thiazolidinediones-2,4 by interaction with monochloroacetic acid or with dimethyl sulfate (with subsequent hydrolysis of the intermediate reaction product).

2. The reaction with dimethyl sulfate may be used to convert 5-arylidenerhodanines into 5-arylidenethiazolidinediones-2,4 and in the case of substances unsubstituted in position 3, the reaction products are methylated simultaneously.

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ORIENTATION DURING SUBSTITUTION IN THE AROMATIC SERIES

V. ISOMERIZATION OF DICHLOROBENZENES

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We previously [1] carried out a series of experiments on the isomerization of dichlorobenzenes at 120-160°. At 160°, a state close to equilibrium between the isomers was reached and the composition of the equilibrium mixture was found. Equilibrium could not be reached, however, at 120°.

In the present work we describe a continuation of experiments on isomerization at 120°, the results of experiments on isomerization at 100 and 180° and experiments with hydrogen chloride introduced into the reaction mixture.

EXPERIMENTAL

The three isomeric dichlorobenzenes were separately heated in sealed tubes with aluminum chloride. The reaction mixture was then poured into acidified water and the dichlorobenzene separated, washed, dried and vacuum distilled. If the distilled product did not solidify at room temperature, then a definite amount of pure para-isomer was added to it to raise the solidification point of the mixture. When the solidification point had been determined, the mixture was nitrated, reduced and brominated as described previously [2] for a complete analysis of the reaction product.

Table 1 gives the results of experiments where the mixtures were heated at 180° and these show that the system reached a state close to equilibrium after 20 hours at this temperature. The system did not reach a state close to equilibrium at 120° after 560 hours or even 1010 hours, and this compelled us to start not from pure isomers but from mixtures close to the assumed equilibrium composition in subsequent experiments. Experiments 5 and 6 showed that at 120°, in mixtures containing 5% of the ortho-isomer before isomerization, its content increased to 10% after 200 hours and in mixtures containing 15%, its content fell to 12.6%. Hence, it follows that the equilibrium mixture contains about 12% of the ortho-isomer, about 55% of the meta-isomer and about 33% of the para-isomer. A comparison of the equilibrium compositions at 120, 160 and 180° shows a certain increase in the ortho-isomer content of the equilibrium mixture at 160-180° and as the ortho- is the most labile isomer, this is in accord with thermodynamic rules. The difference, however, is small, apparently due to the very small heat of conversion of ortho → para or ortho → meta.

An attempt was also made to produce irreversible isomerization when the rate of conversion of the most stable meta-isomer would be practically equal to zero at an appreciable isomerization rate of the others. The results of experiments presented in Table 2, however, shows that irreversible isomerization is impossible at 101° since the difference in the kinetic stability of the isomers is too small for the practical realization of irreversible isomerization.

A series of experiments was carried out to study the effect of hydrogen chloride on the isomerization rate. Thus, in Experiment 3 (Table 2), a drop of water was put onto the inside wall of a tube with a mixture of aluminum chloride (1.526 g) and 0-dichlorobenzene and the tube sealed. Comparison of the results of Experiment 3 with the results of Experiment 4, carried out under the same conditions but without water, shows that with the drop of water, which gives hydrogen chloride with aluminum chloride and partly the complex $H[AlCl_3 \cdot OH]$, isomerization proceeds more slowly.

TABLE 1

Isomerization of Dichlorobenzene in the Presence of 0.27 g mole of Aluminum Chloride (20 weight %)

Expt. No.	Isomer	Temperature	Time (in hr)	Composition of mixture after izomerization (in %)		
				ortho-	para-	meta-
1	Ortho-	180°	15	19.2	28.3	52.5
	Para-			9.3	36.6	54.1
	Meta -			11.2	30.5	58.3
2	Ortho-	180	20	13.6	28.2	56.2
	Para-			14.5	30.7	54.8
	Meta-			12.2	30.6	57.2
3	Ortho	120	561	17.4	24.6	58.0
	Para-			5.1	41.1	53.8
	Meta-			4.0	31.2	64.8
4	Ortho-	120	1010	16.8	29.1	54.1
	Para-			5.2	40.2	54.6
	Meta-			10.4	31.9	57.7
5	Ortho-5.0% Para- 40.0% Meta-55.0%	120	200	10.0	35.4	54.6
6	Ortho-45.0% Para- 35.0% Meta-50.0%	120	200	12.6	31.8	55.6

TABLE 2

Isomerization of Dichlorobenzene at 101° and the Effect of Hydrogen Chloride on the Process

Expt. No.	Reagents		Temp.	Time (in hr)	Composition of mixt. after isomerization (%)			Added to reaction mixture
	dichloro-benzene	moles of $AlCl_3$ per mole of dichloro-benzene			ortho-	para-	meta-	
1	Ortho	0.276	101°	600	63.2	9.9	26.9	—
	Para	0.276			1.2	93.7	7.5	—
	Meta	0.276			—	11.0	—	—
2	Ortho	1.100	101	500	—	18.0	—	—
	Para	1.100			—	69.2	—	—
	Meta	1.100			—	27.2	—	—
3	Ortho	0.510	160	5	53.9	15.1	31.0	A drop of water
4	Par a	0.510	160	5	37.4	21.0	41.6	—
5	Meta	0.276	160	5	81.5	2.9	15.6	Dry HCl passed
6	Ortho	0.276	160	5	57.9	10.4	31.7	—
7	Para	0.276	160	5	70.8	9.8	19.4	0.25 mole of HCl
8	Meta	0.276	160	5	64.8	10.3	24.9	0.10 mole of HCl
9	Ortho	0.276	160	5	53.5	12.3	34.2	—
10	Ortho	1.000	160	5	38.1	24.1	37.8	0.10 mole of HCl
11	Ortho	1.000	160	5	29.1	25.7	45.2	—
12	Ortho	0.276	160	5	62.8	12.6	24.6	HCl HCl absorbed with alkali

In Experiment 5, dry hydrogen chloride was passed through the reaction mixture contained in a vessel with a reflux air condenser. A comparison of the results of the experiment with those of Experiment 6, carried out under the same conditions but with hydrogen chloride, shows that in this case the isomerization proceeds more slowly in the presence of hydrogen chloride. Experiments 5 and 6 were carried out under the same conditions and in both experiments, the aluminum chloride content of the reaction mixture was determined after its conversion to the oxide with ammonia. It was found that 32.2% of the $AlCl_3$ taken remained in the reaction mixture in the experiment with the passage of HCl, while in the experiment without HCl, 76.2% remained. Thus, the stream of hydrogen chloride carried away a large amount of catalyst and this was bound to lower the isomerization rate. Experiments on isomerization with hydrogen chloride were then carried out in sealed tubes. In one arm of an H-shaped vessel was placed o-dichlorobenzene and aluminum chloride and in the other, sulfuric acid and a paraffin wax wafer with sodium chloride. When the vessel had been sealed, the paraffin was melted by heating and the hydrogen chloride liberated.

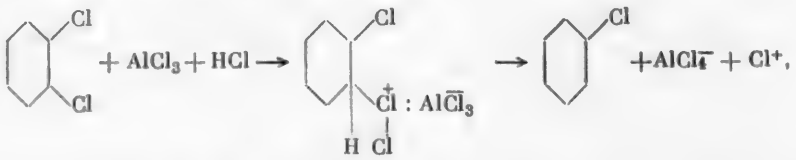
The results of Experiments 7, 8 and 9 show that in this case hydrogen chloride decreases the isomerization rate to a greater extent, the more of it there is introduced. Experiments with 1 mole of $AlCl_3$ to 1 mole of dichlorobenzene gave similar results (see Experiments 10 and 11).

An experiment was then carried out with the removal of hydrogen chloride. Into one arm of an H-shaped tube were placed dichlorobenzene and aluminum chloride and into the other, grains of anhydrous potassium hydroxide and a small tube of phosphorus pentoxide. The sealed vessel was left overnight and then heated. A comparison of the results of this experiment (No. 12) with those of Experiment 9, which was without absorption of the HCl, shows that removal of the small amounts of HCl from the reaction zone also decreases the isomerization rate. Only traces of aluminum were detected in the solid potassium hydroxide after the experiment.

Finally, a method described previously [1] was used to determine the amount of monochlorobenzene in the reaction mixture of an experiment carried out with the ortho-isomer in the presence of 0.27 mole of $AlCl_3$ and 0.25 mole of hydrogen chloride with heating at 160° for 5 hours. The specific gravity of the 1st fraction, equal to 1.2923. showed that chlorobenzene was not present in the reaction mixture.

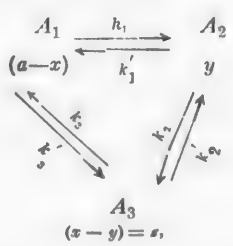
DISCUSSION OF RESULTS

Slowing of the isomerization reaction by appreciable amounts of hydrogen chloride may be explained with reference to the reaction mechanism proposed previously [1]:



where rehalogenation followsdehalogenation. Hydrogen chloride introduced into the system will compete with dichlorobenzene and form a complex with the composition $HalCl_4$. Therefore, the more hydrogen chloride there is introduced, the more the concentration of the complex $C_6H_4Cl_2 \cdot AlCl_3$ will decrease and together with this, the reaction rate will decrease. At the same time, the experiment with the absorption of HCl with alkali showed that small amounts of HCl are necessary for the reaction according to the proposed mechanism. The absence of chlorobenzene from the mixture obtained with hydrogen chloride introduced shows that the dechlorination process is slowed and not the rechlorination. Otherwise, one would expect the accumulation of monochlorobenzene in the mixture.

The experimental material obtained makes it possible to calculate the value of the rate constant of the isomerization reaction and from it, the composition of the mixture at any period of time. Accepting the following conversion scheme



we find:

$$v_1 = \frac{dx}{dt} = k_1(a-x) + k_3'(a-x) - k_1'y - k_3'(x-y) =$$

$$= (k_1 + k_3')a - (k_1 + k_3' + k_3)x - (k_1' - k_3)y.$$

Let us define $(k_1 + k_3')a = M_1$; $k_1 + k_3' + k_3 = M_2$ and $k_1' - k_3 = M_3$,

Then

$$v_1 = \frac{dx}{dt} = M_1 - M_2x - M_3y. \tag{1}$$

Also:

$$v_2 = \frac{dy}{dt} = k_1(a-x) + k_2'(x-y) - k_1'y - k_2y$$

and

$$v_3 = \frac{dz}{dt} = k_3'(a-x) + k_2y - k_3(x-y) - k_2'(x-y).$$

After analogous substitutions we obtain:

$$v_2 = \frac{dy}{dt} = N_1 - N_2x - N_3y \tag{2}$$

$$v_3 = \frac{dz}{dt} = P_1 - P_2x + P_3y,$$

where: $N_1 = k_1a$; $N_2 = k_1 - k_2$; $N_3 = k_2' + k_1' + k_2$ and $P_1 = k_3'a$; $P_2 = k_3' + k_3 + k_2'$; $P_3 = k_2 + k_2' + k_3$.

The rate constants of the isomerization process were determined in the following way. From Equations (1-3) at t = 0 we find:

$$\frac{dx}{dt} = M_1 = (k_1 + k_3')a; \quad \frac{dy}{dt} = N_1 = k_1a; \quad \frac{dz}{dt} = P_1 = k_3'a.$$

The rate was determined from the slope of the initial section of the curve constructed from experimental data, and the values of the constants k_1 and k_3' were calculated. By substituting the second and third isomers as the starting material A_1, we calculate the second and third pairs of constants. In isomerization experiments at 160° in the presence of 0.27 mole of aluminum chloride [1], the following values of the rate constants of the isomerization process were obtained:

$$k_{o\to p} = 0.020; \qquad k_{p\to m} = 0.050;$$
$$k_{p\to o} = 0.010; \qquad k_{o\to m} = 0.056;$$
$$k_{m\to p} = 0.030; \qquad k_{m\to o} = 0.016.$$

To calculate the composition of a mixture from the values of the rate constants found, we solve Equations (1) and (2), which lead to

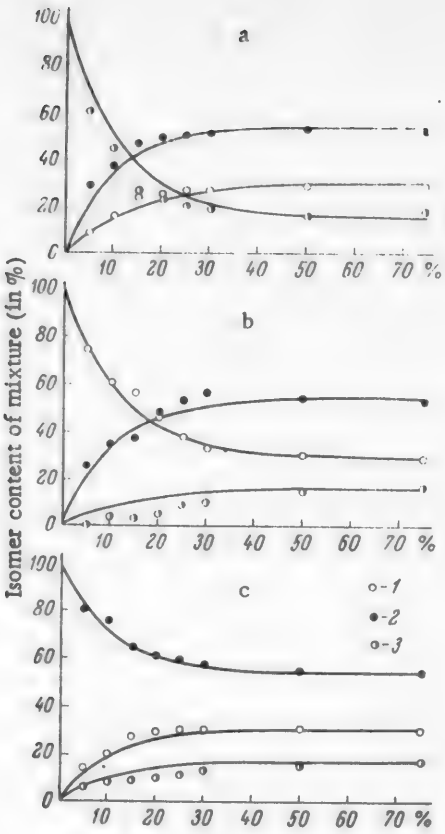
$$x = x_{eq.}\ (1 - e^{\beta t}) + \frac{Q_1}{B}(e^{\alpha t} - e^{\beta t}). \tag{I}$$

Analogously:

$$y = y_{eq.}\ (1 - e^{\beta t}) + \frac{Q_1}{B}(e^{\alpha t} - e^{\beta t}) \tag{II}$$

and

$$z = x - y. \tag{III}$$



Curves of the change in composition of reaction mixtures calculated from the formulas and obtained experimentally [1) para-isomer; 2) meta-isomer; 3) ortho-isomer] for dichlorobenzene [a) ortho; b) para; c) meta].

Here, α and β are the roots of the quadratic equation:

$$\alpha = -\frac{A}{2} + \sqrt{\frac{A^2}{4} + B};$$

$$\beta = -\frac{A}{2} - \sqrt{\frac{A^2}{4} + B},$$

$$A = k_1 + k_2 + k_3 + k_1' + k_2' + k_3', \quad B = N_2M_3 - N_3M_2.$$

On differentiating Equation (I) we obtain:

$$\frac{dx}{dt} = -x_{eq.}\ \beta \cdot e^{\beta t} + \frac{Q_1}{B}(\alpha \cdot e^{\alpha t} - \beta \cdot e^{\beta t}).$$

At t = 0, from

$$\frac{dx}{dt} = -x_{eq.}\ \beta + \frac{Q_1}{B}(\alpha - \beta) = M_1 = (k_1 + k_3')\,a$$

we find the value of the integration constants.

TABLE 3

Constants for the Equilibrium Between Dichlorobenzene Isomers

	Calculated	
	from rate constants	from equilibrium concentrations
para ⇄ ortho	$\frac{0.010}{0.020} = 0.50$	$\frac{16}{30} = 0.53$
para ⇄ meta	$\frac{0.050}{0.030} = 1.67$	$\frac{54}{30} = 1.80$
ortho ⇄ meta	$\frac{0.056}{0.016} = 3.50$	$\frac{54}{16} = 3.38$

In the figure we give the curves of the change in composition of reaction mixtures, calculated from Formulas (I-III). The same figure also shows the experimental results of determining the composition of the mixtures (plotted as points).

The constants for equilibrium between the isomers may be calculated from the rate constants found for isomerization and from the values of the experimental equilibrium concentrations. The results are presented in Table 3.

Thus, we obtained good agreement for the values of the isomer equilibrium constants obtained experimentally and calculated from the compositions of the mixtures.

The composition of an equilibrium mixture of dichlorobenzenes in the gas phase, calculated from thermodynamic functions [3], differs considerably from the equilibrium composition we found for the liquid phase.

SUMMARY

The isomerization of o-, m- and p-dichlorobenzenes at 120 and 180° in the presence of aluminum chloride was studied. It required considerably more than 1000 hours to attain a state of equilibrium between the isomers at 120°. The equilibrium mixture contained about 12% of the ortho-isomer, 33% of the para-isomer and 55% of the meta-isomer. Starting from any isomer, a state close to equilibrium was reached after 20 hours at 180°.

It was found that the rate of the isomerization process decreased when hydrogen chloride was introduced into the reaction vessel and the decrease was greater, the greater the amount introduced. The removal of small amounts of hydrogen chloride from the system also decreased the rate of the isomerization process in accordance with the reaction mechanism proposed.

The rate constants for the isomerization of dichlorobenzenes at 160° were calculated from the experimental data.

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DISCUSSION

PROBLEM OF PREPARING CYCLOHEXADIENE-1,3

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An article was recently published by A. I. Chirko and K. L. Moiseichuk on "The Kinetics of Cyclohexadiene-1,3 Autooxidation" [1]. The authors aimed to prepare cyclohexadiene-1,3 by a previously described method, to develop a new method of preparing it through cyclohexene hydroperoxide and to study the kinetics and products of cyclohexadiene-1,3 autooxidation. The hydrocarbon was obtained by two methods: through cyclohexene hydroperoxide and by the action of quinoline on 1,2-dibromocyclohexane.

A series of investigations has been devoted to the problem of preparing cyclohexadiene-1,3 by the action of quinoline on hexamethylene dibromide. The possibility of forming cyclohexadiene-1,3 by this reaction was first reported in 1892-1898 [2]. Zelinskii and Gorskii [3] considered that the action of 3-4 parts of quinoline on 1 part of 1,2-dibromocyclohexane yielded pure cyclohexadiene-1,3 and the action of a larger amount of quinoline, a mixture of cyclohexadiene-1,3, cyclohexene and 1-bromocyclohexene-1 [4]. Baeyer [2] obtained cyclohexene by the action of quinoline on 1,2-dibromocyclohexane.

While Zelinskii [4] and Crossley [5] considered that the action of quinoline on 1,2-dibromocyclohexane could yield pure cyclohexadiene-1,3 by ozonization and isolating adipodialdehyde, Harries et al. showed that the hydrocarbon obtained by this method contained up to 51% of cyclohexene [6]. In 1912, Willstätter and Hatt [7] isolated (and identified) from the interaction products of 1,2-dibromocyclohexane and quinoline 20 g of benzene, representing 14% of the hydrocarbon fraction, in addition to cyclohexadiene-1,3 and cyclohexene. Later, the formation of benzene by the interaction of these reagents [8] was confirmed spectroscopically and an attempt was made to confirm the mechanism proposed by Domnin [9] for the conversion of halogen derivatives of cyclohexane into aromatic compounds [10].

Thus, the product obtained by heating quinoline with 1,2-dibromocyclohexane was not pure cyclohexadiene-1,3, but was a mixture of cyclohexadiene-1,3, cyclohexene and benzene.

Although Chirko and Moiseichuk, in comparing the physicochemical constants of cyclohexadiene, obtained through cyclohexene hydroperoxide, with this product obtained by Willstätter and Hatt, referred to precisely that article in which Willstätter and Hatt demonstrated the inhomogeneity of the product thus obtained, but did not mention how they freed the cyclohexadiene-1,3 obtained by the action of quinoline on 1,2-dibromocyclohexane, from the accompanying cyclohexene and benzene. Despite the fact that on determining the number of double bonds by Hubley's method the authors obtained the value 2.1, the low refractive index ($n^{20}D$ 1.4640) and density (0.830) of their product indicates that it contained a considerable amount of cyclohexene. In this connection, the question arises as to whether the presence of the latter may explain the lower autooxidation rate observed by the authors for cyclohexadiene-1,3 obtained by the action of quinoline on 1,2-dibromocyclohexane in comparison with cyclohexadiene-1,3 obtained by the first method.

Unfortunately the widely used text book by Gatterman and Wieland also recommends the action of quinoline on 1,2-dibromocyclohexane for the preparation of cyclohexadiene-1,3 [11], though with the reservation that the product contains up to 10-20% of cyclohexene, but without indicating the simultaneous formation of benzene in this reaction.

A series of procedures may be recommended for the preparation of pure cyclohexadiene-1,3, which lead to the formation of a discrete product [12-15].

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